10/ 088,854

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|---|---|---|---|
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| NEWS | 2 | | "Ask CAS" for self-help around the clock |
| NEWS | 3 | SEP 01 | New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover! |
| NEWS | 4 | OCT 28 | KOREAPAT now available on STN |
| NEWS | 5 | NOV 30 | PHAR reloaded with additional data |
| NEWS | 6 | DEC 01 | LISA now available on STN |
| NEWS | 7 | DEC 09 | 12 databases to be removed from STN on December 31, 2004 |
| NEWS | 8 | DEC 15 | MEDLINE update schedule for December 2004 |
| NEWS | 9 | DEC 17 | ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected |
| NEWS | 10 | DEC 17 | COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected |
| NEWS | 11 | DEC 17 | SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected |
| NEWS | 12 | DEC 17 | CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected |
| NEWS | 13 | DEC 17 | THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB |
| NEWS | 14 | DEC 30 | EPFULL: New patent full text database to be available on STN |
| NEWS | 15 | DEC 30 | CAPLUS - PATENT COVERAGE EXPANDED |
| NEWS | 16 | JAN 03 | No connect-hour charges in EPFULL during January and February 2005 |
| NEWS | 17 | JAN 26 | CA/CAPLUS - Expanded patent coverage to include the Russian Agency for Patents and Trademarks (ROSPATENT) |
| NEWS | 18 | FEB 10 | STN Patent Forums to be held in March 2005 |
| NEWS | 19 | FEB 16 | STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005 |

| | |
|---|---|
| NEWS EXPRESS | JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005 |
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| NEWS INTER | General Internet Information |
| NEWS LOGIN | Welcome Banner and News Items |
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| NEWS WWW | CAS World Wide Web Site (general information) |

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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:09:12 ON 23 FEB 2005

=> file reg
COST IN U.S. DOLLARS

| | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 11:09:34 ON 23 FEB 2005
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 22 FEB 2005 HIGHEST RN 835870-69-4
DICTIONARY FILE UPDATES: 22 FEB 2005 HIGHEST RN 835870-69-4

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

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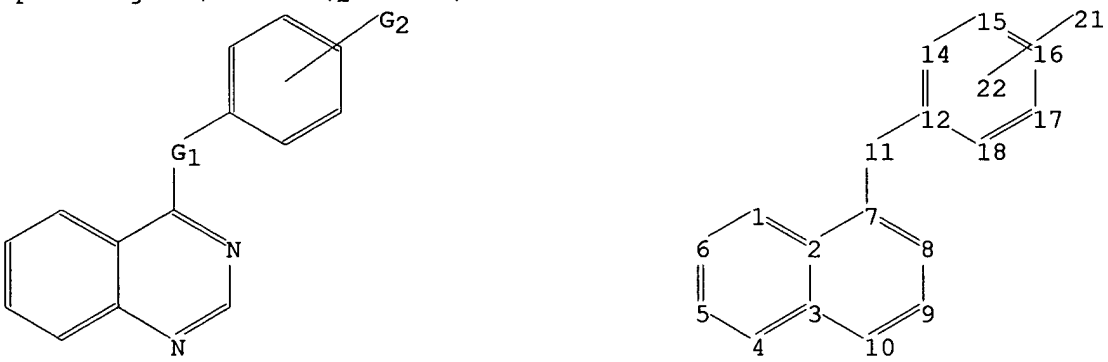
Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\STNEXP4\QUERIES\10088854.str




chain nodes :
11 21
ring nodes :
1 2 3 4 5 6 7 8 9 10 12 14 15 16 17 18
chain bonds :
7-11 11-12
ring bonds :
1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 7-8 8-9 9-10 12-14 12-18 14-15 15-16 16-17 17-18
exact/norm bonds :
7-11 11-12

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normalized bonds :
1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 7-8 8-9 9-10 12-14 12-18 14-15 15-16
16-17 17-18
isolated ring systems :
containing 1 : 12 :

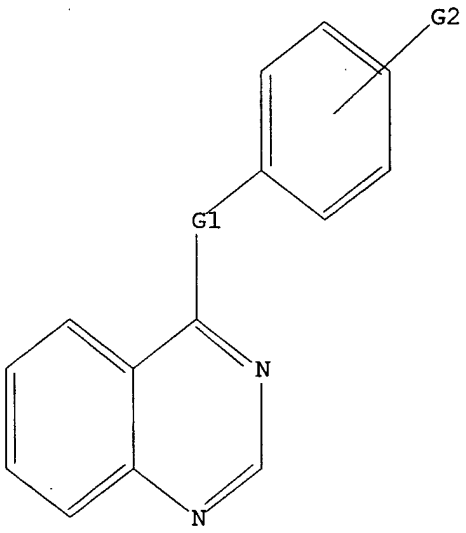
G1:O,S,N,SO2

G2:O,S

Hydrogen count :
9:= exact 1
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS
12:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 21:CLASS 22:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR




G1 O,S,N,SO2
G2 O,S

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sample
SAMPLE SEARCH INITIATED 11:10:14 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 926 TO ITERATE

100.0% PROCESSED 926 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

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BATCH **COMPLETE**
PROJECTED ITERATIONS: 16695 TO 20345
PROJECTED ANSWERS: 2231 TO 3689

L2 50 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 11:10:34 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 19228 TO ITERATE

100.0% PROCESSED 19228 ITERATIONS 3137 ANSWERS
SEARCH TIME: 00.00.01

L3 3137 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 161.76 161.97

FILE 'CAPLUS' ENTERED AT 11:10:58 ON 23 FEB 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


FILE COVERS 1907 - 23 Feb 2005 VOL 142 ISS 9
FILE LAST UPDATED: 22 Feb 2005 (20050222/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3/thu
277 L3
656591 THU/RL
L4 174 L3/THU
(L3 (L) THU/RL)

=> s l4 and (aurora or cancer or tumor or neoplas? or prolifer? or diabetes or alzheimer?)
3248 AURORA
237821 CANCER
328933 TUMOR
398412 NEOPLAS?
211039 PROLIFER?
96525 DIABETES
33479 ALZHEIMER?
L5 107 L4 AND (AURORA OR CANCER OR TUMOR OR NEOPLAS? OR PROLIFER? OR DIABETES OR ALZHEIMER?)

=> d l5 1- ibib abs fhitstr

L5 ANSWER 1 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:120678 CAPLUS
TITLE: Treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment
INVENTOR(S): Spector, Neil Lee; Xia, Wenle
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005011607 | A2 | 20050210 | WO 2004-US24888 | 20040802 |

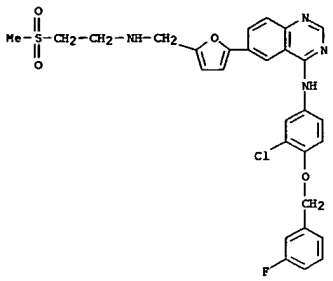
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-491752P P 20030801

AB The truncated ErbB2 receptor (p95ErbB2) is shown to differ from the full-length ErbB2 receptor in its association with other ErbB receptors. The truncated receptor preferentially associated with ErbB3, whereas full length ErbB2 heterodimerizes with either EGFR or ErbB3. Consistent with p95ErbB2 heterodimerization with ErbB3, it is shown that heregulin (an ErbB3 ligand) stimulates p95ErbB2 phosphorylation in breast **cancer** cell lines. Described herein are methods of identifying patients suitable for treatment with a p95ErbB2 inhibitor, and methods of treating such patients. GW572016, a p95ErbB2 inhibitor, inhibited both p95ErbB2 and p185ErbB2 in breast **cancer** xenografts.

IT INDEXING IN PROGRESS
IT **231277-92-2**, GW572016
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(as p95 ErbB2 inhibitor; treatment of cancers expressing p95 ErbB2 with p95 ErbB2 inhibitor and identifying cancers suitable for such treatment)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 1 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L5 ANSWER 2 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:29316 CAPLUS
DOCUMENT NUMBER: 142:134612
TITLE: Preparation of 4-arylaminoquinazolines and analogs as activators of caspases and inducers of apoptosis
INVENTOR(S): Cai, Sui Xiong; Sirisoma, Nilantha Sudath; Pervin, Azra; Drewe, John A.; Kasibhatla, Shailaja; Jaing, Songchun; Zhang, Hong; Pleiman, Chris; Baichwal, Vijay; Manfredi, John; Bhoite, Leena
PATENT ASSIGNEE(S): Myriad Genetics, Inc., USA; Cytovia, Inc.
SOURCE: PCT Int. Appl., 289 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005003100 | A2 | 20050113 | WO 2004-US21631 | 20040706 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-484325P P 20030703
US 2003-493006P P 20030807
US 2004-557556P P 20040329
US 2004-571288P P 20040514

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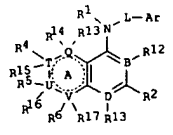

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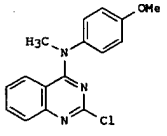


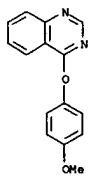
II

AB 4-Arylaminoquinazolines and analogs I [wherein A = 6-membered (hetero)aryl or carbocycle; L = [C(RL1)(RL2)]n or -N(RL1)C(O)-; RL1, RL2 = H or alkyl; n = 0-2; R1 = Me or ethyl; Ar = (un)substituted (hetero)aryl; R2-R6, R12-R17 = H, halo, N3, OH, thiol, nitro, CN, NH2, alk(en/yn)yl or alkoxy; B, D, Q, T, U, V = C or N, wherein at least one of B and D is N; etc. or pharmaceutically acceptable salts or solvates thereof] were prepared as activators of caspases and inducers of apoptosis. For example, 2,4-quinazolinedione was refluxed with neat phosphorylchloride to give 2,4-dichloroquinazoline in 96% yield, which was coupled with 4-methoxy-N-methylaniline to afford II in 87% yield. II exhibited caspase activation (EC50 2 nM for human breast **cancer** cell line T-47D,

L5 ANSWER 2 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

24 h), inhibition of cell **proliferation** (GI50 8 nM for T-47D), inhibition of tubulin polymn. (IC50 <500 nM) and cytotoxicity in multidrug resistant cells (IC50 2.9 nM for MCF-7 cell line). Other biol. activities of the invented compds. have also been tested. Therefore, I and pharmaceutical compns. thereof (examples given) are effective activators of caspases and inducers of apoptosis, and useful in the treatment of such as **cancer**, autoimmune and inflammation. Disclosed are 4-arylaminoquinazolines and analogs thereof effective as activators of caspases and inducers of apoptosis.

IT **93866-13-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of arylaminoquinazolines and analogs as activators of caspases and inducers of apoptosis)
RN 93866-13-8 CAPLUS
CN Quinazoline, 4-(p-methoxyphenoxy)- (7CI) (CA INDEX NAME)



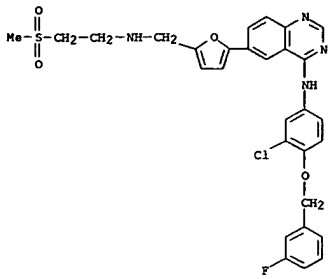
L5 ANSWER 3 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:19225 CAPLUS
DOCUMENT NUMBER: 142:126886
TITLE: The dual ErbB1/ErbB2 inhibitor, lapatinib (GW572016), cooperates with tamoxifen to inhibit both cell proliferation- and estrogen-dependent gene expression in antiestrogen-resistant breast cancer
AUTHOR(S): Chu, Isabel; Blackwell, Kimberly; Chen, Susie; Slingerland, Joyce
CORPORATE SOURCE: The Braman Breast Cancer Institute, UM Sylvester Comprehensive Cancer Center, University of Miami School of Medicine, Miami, FL, USA
SOURCE: Cancer Research (2005), 65(1), 18-25
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Effective treatment of estrogen receptor (ER)-pos. breast cancers with tamoxifen is often curtailed by the development of drug resistance. Antiestrogen-resistant breast cancers often show increased expression of the epidermal growth factor receptor family members, ErbB1 and ErbB2. Tamoxifen activates the cyclin-dependent kinase inhibitor, p27 to mediate G1 arrest. ErbB2 or ErbB1 overexpression can abrogate tamoxifen sensitivity in breast cancer lines through both reduction in p27 levels and inhibition of its function. Here we show that the dual ErbB1/ErbB2 inhibitor, lapatinib (GW572016), can restore tamoxifen sensitivity in ER-pos., tamoxifen-resistant breast cancer models. Treatment of MCF-7pr, T-47D, and ZR-75 cells with lapatinib or tamoxifen alone caused an incomplete cell cycle arrest. Treatment with both drugs led to a more rapid and profound cell cycle arrest in all three lines. Mitogen-activated protein kinase and protein kinase B were inhibited by lapatinib. The two drugs together caused a greater reduction of cyclin D1 and a greater p27 increase and cyclin E-cdk2 inhibition than observed with either drug alone. In addition to inhibiting mitogenic signaling and cell cycle progression, lapatinib inhibited estrogen-stimulated ER transcriptional activity and cooperated with tamoxifen to further reduce ER-dependent transcription. Lapatinib in combination with tamoxifen effectively inhibited the growth of tamoxifen-resistant ErbB2 overexpressing MCF-7 mammary tumor xenografts. These data provide strong preclin. data to support clin. trials of ErbB1/ErbB2 inhibitors in combination with tamoxifen in the treatment of human breast cancer.

IT **231277-92-2**, Lapatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual ErbB1/ErbB2 inhibitor, lapatinib (GW572016), cooperates with tamoxifen to inhibit both cell proliferation- and estrogen-dependent gene expression in antiestrogen-resistant breast cancer)

RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 3 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1038664 CAPLUS
DOCUMENT NUMBER: 142:6556
TITLE: Preparation of substituted heterocycles for the treatment of abnormal cell growth
INVENTOR(S): Bhattacharya, Samit Kumar; Chen, Jinshan; Connell, Richard Damian; Kath, John Charles; Kauffman, Goss S.; Lippa, Blaise S.; Morris, Joel
PATENT ASSIGNEE(S): Pfizer Inc, USA
SOURCE: U.S. Pat. Appl. Publ., 54 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004242604 | A1 | 20041202 | US 2004-849707 | 20040520 |
| WO 2004106308 | A1 | 20041209 | WO 2004-IB1687 | 20040517 |

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-473817P P 20030527
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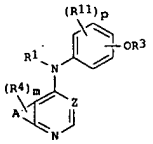


I

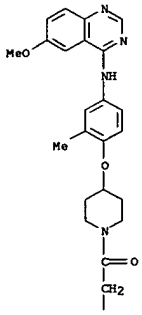
AB Title compds. I [Z = CR1, CCN, N; A = fused 5-7-membered ring optionally containing heteroatoms; R1 = H, alkyl; m = 0-3; p = 0-4; R3 = Ph, 4-6-membered heterocyclic ring; R4 = substituted divalent alkyl, etc.; R11 = halo, CN, NO2, etc.] are prepared For instance, N-tert-Butyl-4-[[2-methyl-4-[(6-(morpholin-4-yl)pyrido[3,4-d]pyrimidin-4-yl)amino]phenyl]oxy]benzamide is prepared in 8 steps from 6-fluoro-3H-pyrido[3,4-d]pyrimidin-4-one and 3-(4-amino-2-methylphenoxy)benzoic acid tert-Bu ester. Compds. of the invention have IC50 values of <10 μM against erbB-2 kinase. I are useful for treating abnormal cell growth.

IT **799242-37-8P**, 2-Cyclopropyl-1-[4-[[4-[(6-methoxyquinazolin-4-yl)amino]-2-methylphenyl]oxy]piperidin-1-yl]ethanone
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); THU (Therapeutic use); BIOL (Biological study); PREP

L5 ANSWER 4 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
(Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of substituted pyrimidine/quinazolines for treatment of abnormal cell growth)

RN 799242-37-8 CAPLUS
CN Piperidine, 1-(cyclopropylacetyl)-4-[4-[(6-methoxy-4-quinazolinyl)amino]-2-methylphenoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



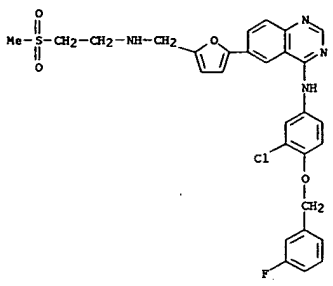
PAGE 2-A

L5 ANSWER 5 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:999609 CAPLUS
DOCUMENT NUMBER: 141:420612
TITLE: ErbB surface receptor complexes as biomarkers in determining disease
INVENTOR(S): Chan-Hui, Po-Ying; Dua, Rajiv; Mukherjee, Ali; Pidaparthi, Sailaja; Salimi-Moosavi, Hossein; Shi, Yining; Singh, Sharat
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 67 pp., Cont.-in-part of U.S. Ser. No. 623,057.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 29
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004229294 | A1 | 20041118 | US 2004-813417 | 20040330 |
| US 2003013126 | A1 | 20030116 | US 2002-154042 | 20020521 |
| US 2004126818 | A1 | 20040701 | US 2003-623057 | 20030717 |
| PRIORITY APPLN. INFO.: | | | US 2002-154042 | A2 20020521 |
| | | | US 2003-459888P | P 20030401 |
| | | | US 2003-623057 | A2 20030717 |
| | | | US 2003-494482P | P 20030811 |
| | | | US 2003-508034P | P 20031001 |
| | | | US 2003-512941P | P 20031020 |
| | | | US 2003-523258P | P 20031118 |
| | | | US 2001-292548P | P 20010521 |
| | | | US 2001-334901P | P 20011024 |
| | | | US 2002-398724P | P 20020725 |

AB The invention is directed to a new class of biomarker in patient samples comprising dimers of ErbB cell surface membrane receptors. In one aspect, the invention includes a method of determining the status of a disease or healthful condition by correlating such condition to amts. of one or more dimers of ErbB cell surface membrane receptors measured directly in a patient sample, in particular a fixed tissue sample. In another aspect, the invention includes a method of determining a status of a **cancer** in a specimen from an individual by correlating measurements of amts. of one or more dimers of ErbB cell surface membrane receptors in cells of the specimen to such status, including presence or absence of a pre-cancerous state, presence or absence of a cancerous state, prognosis of a **cancer**, or responsiveness to treatment. Preferably, methods of the invention are implemented by using sets of binding compds. having releasable mol. tags that are specific for multiple components of one or more types of receptor dimers. After binding, mol. tags are released and separated from the assay mixture for anal.
IT **231277-92-2**, GW572016
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(ErbB-dimer acting drugs; ErbB surface receptor complexes as biomarkers in determining disease)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 5 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

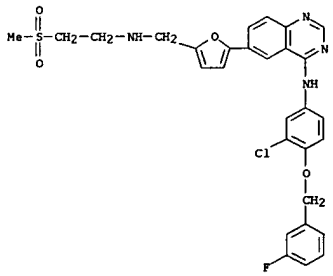


L5 ANSWER 6 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:995727 CAPLUS
DOCUMENT NUMBER: 141:420611
TITLE: ErbB heterodimers as biomarkers for determining disease status and for selecting patients for treatment with ErbB dimer acting drugs
INVENTOR(S): Chan-hui, Po-Ying; Dua, Rajiv; Mukherjee, Ali; Pidaparthi, Sailaja; Salimi-Moosavi, Hossein; Shi, Yining; Singh, Sharat
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 65 pp., Cont.-in-part of U.S. Ser. No. 623,057.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 29
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004229380 | A1 | 20041118 | US 2004-813412 | 20040330 |
| US 2003013126 | A1 | 20030116 | US 2002-154042 | 20020521 |
| US 2004126818 | A1 | 20040701 | US 2003-623057 | 20030717 |
| PRIORITY APPLN. INFO.: | | | US 2002-154042 | A2 20020521 |
| | | | US 2003-623057 | A2 20030717 |
| | | | US 2003-494482P | P 20030811 |
| | | | US 2003-508034P | P 20031001 |
| | | | US 2003-512941P | P 20031020 |
| | | | US 2003-523258P | P 20031118 |
| | | | US 2001-292548P | P 20010521 |
| | | | US 2001-334901P | P 20011024 |
| | | | US 2002-398724P | P 20020725 |

AB The invention is directed to a new class of biomarker in patient samples comprising heterodimers of Her cell surface membrane receptors. In one aspect, the invention includes a method of determining the status of a disease or healthful condition by correlating such condition to amts. of one or more heterodimers of ErbB or Her cell surface membrane receptors measured directly in a patient sample, in particular a fixed tissue sample. In another aspect, the invention includes a method of determining a status of a **cancer** in a specimen from an individual by correlating measurements of amts. of one or more heterodimers of ErbB cell surface membrane receptors in cells of the specimen to such status, including presence or absence of a pre-cancerous state, presence or absence of a cancerous state, prognosis of a **cancer**, or responsiveness to treatment. Preferably, methods of the invention are implemented by using sets of binding compds. having releasable mol. tags that are specific for multiple components of one or more types of receptor dimers. After binding, mol. tags are released and separated from the assay mixture for anal.
IT **231277-92-2**, GW572016
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(ErbB heterodimers as biomarkers for determining disease status and for selecting patients for treatment with ErbB dimer-acting drugs)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

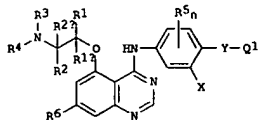
L5 ANSWER 6 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



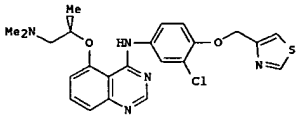
L5 ANSWER 7 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:927050 CAPLUS
DOCUMENT NUMBER: 141:395568
TITLE: Preparation of (anilino)quinazoline derivatives as antiproliferative agents
INVENTOR(S): Bradbury, Robert Hugh; Kettle, Jason Grant
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004093880 | A1 | 20041104 | WO 2004-GB1713 | 20040420 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: GB 2003-9009 A 20030422
OTHER SOURCE(S): MARPAT 141:395568
GI



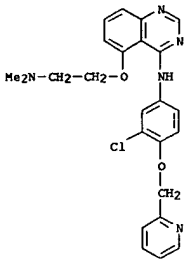
I



II

AB Title compds. represented by the formula I [wherein R1, R2 = independently H, carboxy, formyl, etc.; R1a, R2a = independently H or alkyl; R3, R4 =

L5 ANSWER 7 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
independently H, alkyl, alkenyl; R5 = halo, OH, alkyl, alkoxy, alkenyl, alkynyl; R6 = H, alkoxy, alkenyloxy, alkynyloxy; X = H, halo, alkyl, alkoxy, alkenyl, alkynyl; Y = O, S, SO2, etc.; Q1 = Ph, pyridinyl, pyrazinyl, etc.; and pharmaceutically acceptable salts thereof] were prepd. as antiproliferative agents. For example, reaction of 2-chloro-4-[[5-[(1R)-2-dimethylamino-1-methylethoxy]quinazolin-4-yl]amino]phenol with 4-(chloromethyl)thiazole•HCl gave II in 20% yield. II showed inhibition of phosphorylation of a tyrosine contg. polypeptide substance by ERBB2 kinase (IC50 = 0.002 μM), EGFR kinase (IC50 = 0.068 μM) and ERBB2 in a MCF6 (breast carcinoma) derived cell line (IC50 = 0.001 μM). Thus, I and their pharmaceutical compns. are useful as antiproliferative agents in the prodn. of an ERBB2 receptor tyrosine kinase inhibitory effect in a warm-blooded animal such as man.
IT 786688-99-1P, 4-[3-Chloro-4-(2-pyridylmethoxy)anilino]-5-(2-dimethylaminoethoxY)quinazoline
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-anilino-quinazoline derivs. as antiproliferative agents)
RN 786688-99-1 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-(2-pyridinylmethoxy)phenyl]-5-[2-(dimethylamino)ethoxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

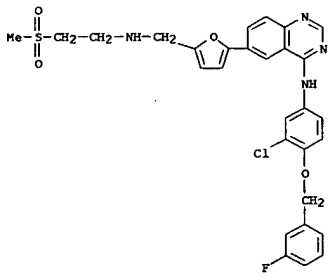
L5 ANSWER 8 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:902075 CAPLUS
DOCUMENT NUMBER: 141:361105
TITLE: Methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof
INVENTOR(S): Chan-Hui, Po-Ying; Salimi-Moosavi, Hossein; Shi, Yining; Singh, Sharat; Dua, Rajiv; Mukherjee, Ali; Pidaparthi, Sailaja
PATENT ASSIGNEE(S): Aclara Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 29
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004091384 | A2 | 20041028 | WO 2004-US9715 | 20040330 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004126818 | A1 | 20040701 | US 2003-623057 | 20030717 |

PRIORITY APPLN. INFO.:
US 2003-459888P P 20030401
US 2003-623057 A 20030717
US 2003-494482P P 20030811
US 2003-508034P P 20031001
US 2003-512941P P 20031020
US 2003-523258P P 20031118
US 2002-398724P P 20020725

AB The invention is directed to a new class of biomarker in patient samples comprising dimers of ErbB cell surface membrane receptors. In one aspect, the invention includes a method of determining the status of a disease or healthful condition by correlating such condition to amts. of one or more dimers of ErbB cell surface membrane receptors measured directly in a patient sample, in particular a fixed tissue sample. In another aspect, the invention includes a method of determining a status of a cancer in a specimen from an individual by correlating measurements of amts. of one or more dimers of ErbB cell surface membrane receptors in cells of the specimen to such status, including presence or absence of a pre-cancerous state, presence or absence of a cancerous state, prognosis of a cancer, or responsiveness to treatment. Preferably, methods of the invention are implemented by using sets of binding compds. having releasable mol. tags that are specific for multiple components of one or more types of receptor dimers. After binding, mol. tags are released and separated from the assay mixture for anal.
IT 231277-92-2, GW572016
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for detection of ErbB cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof)

L5 ANSWER 8 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 9 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

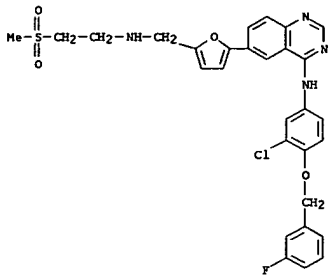
ACCESSION NUMBER: 2004:757696 CAPLUS
DOCUMENT NUMBER: 141:253987
TITLE: A Unique Structure for Epidermal Growth Factor Receptor Bound to GW572016 (Lapatinib): Relationships among Protein Conformation, Inhibitor Off-Rate, and Receptor Activity in Tumor Cells
AUTHOR(S): Wood, Edgar R.; Truesdale, Anne T.; McDonald, Octerloney B.; Yuan, Derek; Hassell, Anne; Dickerson, Scott H.; Ellis, Byron; Pennisi, Christopher; Horne, Earnest; Lackey, Karen; Alligood, Krystal J.; Rusnak, David W.; Gilmer, Tona M.; Shewchuk, Lisa
CORPORATE SOURCE: Departments of Computational, Analytical and Structural Sciences, Assay Development and Compound Profiling, Gene Expression and Protein Biochemistry, High-Throughput Chemistry, and Oncology Biology, GlaxoSmithKline, Inc., Research Triangle Park, NC, 27709-13398, USA
SOURCE: Cancer Research (2004), 64(18), 6652-6659
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB GW572016 (Lapatinib) is a tyrosine kinase inhibitor in clin. development for cancer that is a potent dual inhibitor of epidermal growth factor receptor (EGFR, ErbB-1) and ErbB-2. The authors determined the crystal structure of EGFR bound to GW572016. The compound is bound to an inactive-like conformation of EGFR that is very different from the active-like structure bound by the selective EGFR inhibitor OSI-774 (Tarceva) described previously. Surprisingly, the authors found that GW572016 has a very slow off-rate from the purified intracellular domains of EGFR and ErbB-2 compared with OSI-774 and another EGFR selective inhibitor, ZD-1839 (Iressa). Treatment of tumor cells with these inhibitors results in down-regulation of receptor tyrosine phosphorylation. The authors evaluated the duration of the drug effect after washing away free compound and found that the rate of recovery of receptor phosphorylation in the tumor cells reflected the inhibitor off-rate from the purified intracellular domain. The slow off-rate of GW572016 correlates with a prolonged down-regulation of receptor tyrosine phosphorylation in tumor cells. The differences in the off-rates of these drugs and the ability of GW572016 to inhibit ErbB-2 can be explained by the enzyme-inhibitor structures.

IT 231277-92-2D, Lapatinib, complexes with EGFR
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(unique structure for epidermal growth factor receptor bound to GW572016 (Lapatinib) and relationships among protein conformation, inhibitor off-rate, and receptor activity in tumor cells)

RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 9 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:681496 CAPLUS
DOCUMENT NUMBER: 141:207223
TITLE: Preparation of quinolines and quinazolines, in particular (quinazolin-4-yl)aminophenylethanone oximes, as anticancer agents
INVENTOR(S): Vedula, Manohar Sharma; Kattuboina, Venkata Adiseshu; Iqbal, Javed; Ramanujam, Rajagopalan; Rajagopal, Sriram; Mamidi, Naga Venkata Srinivasa Rao; Josyula, Ramanatham; Gutta, Madhusudhan
PATENT ASSIGNEE(S): Reddy's Laboratories Ltd., India
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004069145 | A2 | 20040819 | WO 2004-IB299 | 20040206 |
| WO 2004069145 | A3 | 20041216 | | |

W: AE, AE, AG, AL, AL, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IN 2003-MA108 A 20030207
OTHER SOURCE(S): MARPAT 141:207223
GI

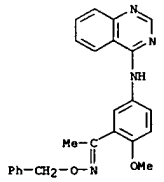
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein R1, R2 = H, halo, OH, NO2, CN, NH2, (un)substituted cyclo/ar/heteroar/heterocyclyl/alkyl, cyclo/alkoxy, acyl, acyloxy, hetero/aryl, aryloxy, alkylthio, arylthio, alkenyl, aroyl, heteroaryloxy, arylcarbonyl, CO2H and derivs., etc.; R3 = H, halo, OH, CN, NH2, CH2CN, (un)substituted cyclo/alkyl, ar/cyclo/alkoxy, hetero/aryl, aryloxy, acyl, CO2H and derivs., etc.; R4, R5, R6 = independently H, halo, OH, NO2, CN, NH2, (un)substituted ar/cyclo/alkyl, cyclo/alkoxy, hetero/aryl, acyl, CO2H and derivs., etc.; W = (un)substituted Ph, naphthyl, pyrrolyl, pyridyl, quinolinyl, benzofuryl, dihydrobenzofuryl, benzopyranyl, dihydrobenzopyranyl, indolyl, indolinyl, azaindolyl, azaindolinyl, pyrazolyl, benzothiazolyl, benzoxazolyl, and the like; Q = N, CH, C; Y = O, NH, CH2; X = (O)r; Z = (CH2)s; T = (CH2)t; U = (O)u; s, t = 0-5; r, u = 0-1; their pharmaceutically acceptable salts, and their geometrical isomers; with provisos] were prepared as anticancer agents. A 3-step synthesis for quinazoline II is given. Selected I displayed potent antiproliferative activity in the human tumor lines with GI50 values at 48 h for MCF 7 (3-5 μM), SW 620 (3-5 μM), and H522 (3 μM) and SKOV3 (2-7 μM) cell lines.

L5 ANSWER 10 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

IT 741275-77-4P, 1-[2-Methoxy-5-(quinazolin-4-ylamino)phenyl]ethanone O-benzyloxime
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor agent; preparation of quinolines and quinazolines, in particular (quinazolin-4-yl)aminophenylethanone oximes, as antitumor agents)

RN 741275-77-4 CAPLUS
CN Ethanone, 1-[2-methoxy-5-(4-quinazolinylamino)phenyl]-, O-(phenylmethyl)oxime (9CI) (CA INDEX NAME)



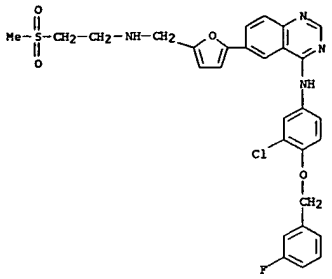
L5 ANSWER 11 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:557096 CAPLUS
DOCUMENT NUMBER: 141:150341
TITLE: Dual kinase inhibition in the treatment of breast cancer: initial experience with the EGFR/ErbB-2 inhibitor lapatinib
AUTHOR(S): Burris, Howard A., III
CORPORATE SOURCE: Sarah Cannon Cancer Center and Tennessee Oncology, Nashville, TN, USA
SOURCE: Oncologist (2004), 9(Suppl. 3), 10-15
CODEN: OCOLF6; ISSN: 1083-7159
PUBLISHER: AlphaMed Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Dual inhibition of ErbB-1 (EGFR) and ErbB-2 (HER-2) tyrosine kinases has been found to exert greater biol. effects in the inhibition of signaling pathways promoting **cancer** cell **proliferation** and survival than inhibition of either receptor alone. The novel dual EGFR/ErbB-2 tyrosine kinase inhibitor lapatinib (GlaxoSmithKline; Research Triangle Park, NC) has been shown to inhibit **tumor** cell growth in vitro and in xenograft models for a variety of human tumors. Preliminary findings in a phase I study of lapatinib in patients with solid tumors indicate doses up to 1,800 mg per day are well tolerated. No grade 4 toxicities were observed and only two of 43 patients had grade 3 toxicity (diarrhea). Clin. activity of lapatinib was observed in these patients; nine patients with a variety of tumors remained on study for ≥4 mo, one with a complete response (head and neck **cancer**). In a phase IB study in pretreated metastatic **cancer** patients with disease that could be biopsied, grade 1 or 2 diarrhea and rash were the most common adverse events. Three patients with breast **cancer** refractory to trastuzumab (Herceptin; Genentech, Inc.; South San Francisco, CA) had partial responses and 12 patients with a variety of tumors had stable disease. Assessment of biol. correlates in these patients indicates that increased **tumor** cell apoptosis on the terminal deoxynucleotide transferase-mediated dUTP nick-end labeling assay correlates with clin. response. Lapatinib currently is being evaluated in phase II and phase III trials in patients with metastatic breast **cancer**.

IT **231277-92-2**, Lapatinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(EGFR/ErbB-2 kinase inhibitor lapatinib in treatment of breast **cancer**)

RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 11 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

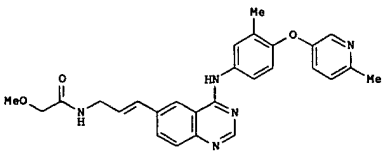


REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

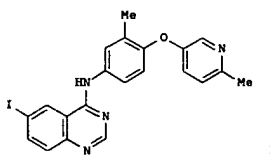
L5 ANSWER 12 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:546496 CAPLUS
DOCUMENT NUMBER: 141:106484
TITLE: A preparation of complexes of quinazoline derivative, useful as selective erbB2 inhibitors
INVENTOR(S): Li, Zheng Jane; Leonard, Jason Albert; Trask, Andrew Vincent; Kath, John Charles; Richter, Daniel Tyler; Thompson, Carl Brian; Morris, Joel
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004056802 | A1 | 20040708 | WO 2003-IB5783 | 20031208 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| NL 1025072 | A1 | 20040622 | NL 2003-1025072 | 20031218 |
| PRIORITY APPLN. INFO.: | | | US 2002-434700P P | 20021219 |

GI



I



II

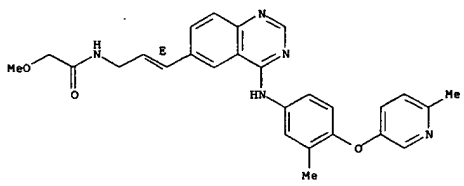
AB The invention relates to a preparation of complexes of quinazoline derivative of

L5 ANSWER 12 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
formula I. The invention also relates to pharmaceutical compns. contg. the complexes of formula I. The invention further relates to methods of treating hyperproliferative diseases, such as cancers, in mammals, esp. humans by administering the above complexes and to methods of prepg. the above complexes. Compd. I was prepd. via Suzuki coupling of 2-methoxyacetic acid propargylamide and quinazoline deriv. II with a yield of 59%.

IT **719270-48-1P**
RL: PAC (Pharmacological activity); PRP (Properties); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline derivative complexes, useful as selective erbB2 inhibitors)

RN 719270-48-1 CAPLUS
CN Acetamide, 2-methoxy-N-[(2E)-3-[4-[[3-methyl-4-[(6-methyl-3-pyridinyl)oxy]phenyl]amino]-6-quinazolinyl]-2-propenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



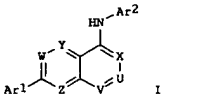
● HCl

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

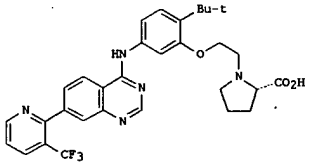
L5 ANSWER 13 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:534192 CAPLUS
DOCUMENT NUMBER: 141:89101
TITLE: Preparation of carboxylic acid, phosphate, or phosphonate substituted (quinazolin-4-yl)amines as capsaicin receptor modulators
INVENTOR(S): Bakthavatchalam, Rajagopal; Blum, Charles A.; Brielmann, Harry; Caldwell, Timothy M.; De Lombaert, Stephane; Hodgetts, Kevin J.; Zheng, Xiaozhang
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004055004 | A1 | 20040701 | WO 2003-US39607 | 20031212 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004156869 | A1 | 20040812 | US 2003-735607 | 20031212 |
| PRIORITY APPLN. INFO.: | | | US 2002-433139P P | 20021213 |
| OTHER SOURCE(S): | | | MARPAT 141:89101 | |

GI



I



II

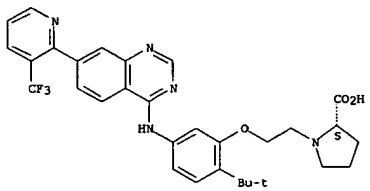
L5 ANSWER 13 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

AB Title acid-substituted (quinazolin-4-yl)amines and analogs (I) [wherein V, W, X, Y, and Z = independently N, CR1, with the proviso that at least one of V and X = N; U = N, CR2, with the proviso that if V and X = N, then U = CR2; R1 = independently H, halo, OH, CN, NH2, CO2H, (halo)alkyl, (halo)alkoxy, alkoxycarbonyl, (di)alkylamino; R2 = H, halo, CN, NO2, (un)substituted alkyl, alkenyl, or alkynyl optionally interrupted by O, S, SO, SO2, CO, OCO, CO2, OCO2, CHNH, NHCO, NHSO2, SO2NH, NH, OPO2(OH), or PO2(OH); Ar1 and Ar2 = independently (un)substituted carbocyclyl, heterocyclyl; and pharmaceutically acceptable forms thereof] were prepared as modulators of capsaicin receptors, especially the vanilloid receptor 1 (VR1). For example, 2-tert-butyl-5-nitrophenol was condensed with 2-(tert-butyldimethylsilyloxy)ethanol, and the resulting nitrophenyl ether reduced to give the substituted aniline. Condensation of the phenylamine with 4-chloro-7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-ol, followed by deprotection, coupling with L-proline Me ester, and saponification provided II. In competition binding assays, invention compds. exhibited Ki ≤ 1 μM for VR1 expressed in human embryonic kidney (HEK293) cells. Thus, I and their pharmaceutical comprns. are useful for treating disorders associated with pathol. receptor activation, such as pain, in humans, domesticated companion animals, and livestock animals (no data).

IT **714956-49-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(VR1 inhibitor; preparation of acid-substituted (quinazolin-4-yl)amines as VR1 inhibitors for treatment of pain and other VR1-mediated conditions)

RN 714956-49-7 CAPLUS
CN L-Proline, 1-[2-[2-(1,1-dimethylethyl)-5-[[7-[3-(trifluoromethyl)-2-pyridinyl]-4-quinazolinyl]amino]phenoxy]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

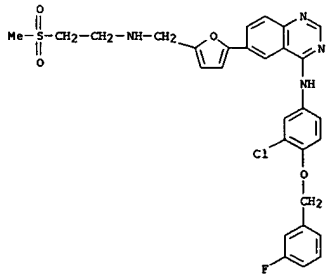
L5 ANSWER 14 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:533970 CAPLUS
DOCUMENT NUMBER: 141:65088
TITLE: Methods and compositions for the prevention or treatment of **neoplasia** comprising a COX-2 inhibitor in combination with an epidermal growth factor receptor antagonist
INVENTOR(S): Masferrer, Jaime
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 103 pp., Cont.-in-part of U.S. Ser. No. 470,951.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004127470 | A1 | 20040701 | US 2003-651916 | 20030829 |
| PRIORITY APPLN. INFO.: | | | US 1998-113786P P | 19981223 |
| | | | US 1999-470951 B2 | 19991222 |

AB The present invention relates to a novel method of preventing and/or treating **neoplasia** disorders in a subject that is in need of such prevention or treatment by administering to the subject at least one COX-2 inhibitor in combination with an EGF receptor antagonist. Comprns., pharmaceutical comprns. and kits are also described.

IT **231277-92-2**, GW572016
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(as EGFR antagonist; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of **neoplasia**)

RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 14 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L5 ANSWER 15 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:533967 CAPLUS
DOCUMENT NUMBER: 141:65147
TITLE: Method for treating diseases associated with abnormal tyrosine kinase activity by administering a DNA methylation inhibitor and a tyrosine kinase inhibitor
INVENTOR(S): Lyons, John; Rubinfeld, Joseph
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of U.S. Ser. No. -71,849.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004127453 | A1 | 20040701 | US 2002-206854 | 20020726 |
| US 2003147813 | A1 | 20030807 | US 2002-71849 | 20020207 |
| WO 2003065995 | A2 | 20030814 | WO 2003-US3537 | 20030206 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

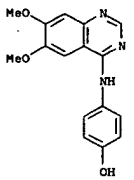
PRIORITY APPLN. INFO.: US 2002-71849 A2 20020207
US 2002-206854 A1 20020726

AB Methods are provided for treating diseases associated with abnormal activity of kinases. The method comprises: administering a DNA methylation inhibitor to the patient in therapeutically effective amount; and administering a kinase inhibitor to the patient in therapeutically effective amount, such that the in vivo activity of the kinase is reduced relative to that prior to the treatment. The method can be used to treat cancer associated with abnormal activity of kinases such as phosphatidylinositol 3'-kinase (PI3K), protein kinases including serine/threonine kinases such as Raf kinases, protein kinase kinases such as MEK, and tyrosine kinases such as those in the epidermal growth factor receptor family (EGFR), platelet-derived growth factor receptor family (PDGFR), vascular endothelial growth factor receptor (VEGFR) family, nerve growth factor receptor family (NGFR), fibroblast growth factor receptor family (FGFR) insulin receptor family, ephrin receptor family, Met family, Ror family, c-kit family, Src family, Fes family, JAK family, Fak family, Btk family, Syk/ZAP-70 family, and Abl family.

IT **202475-60-3**, 4-(4'-Hydroxyphenyl)amino-6,7-dimethoxyquinazoline
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(as Jak inhibitor; treating diseases associated with abnormal tyrosine kinase activity by administering DNA methylation inhibitors and tyrosine kinase inhibitors)

RN 202475-60-3 CAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 15 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L5 ANSWER 16 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:531364 CAPLUS
DOCUMENT NUMBER: 141:89096
TITLE: A microbial preparation of 4-anilinoquinazoline derivatives, useful for the treatment of abnormal cell growth
INVENTOR(S): Kath, John Charles; Liu, Zhengyu; Brown, Maria Steflik; Winter, Steven Mark; Truesdell, Susan Jane; Szewc, Ruby Anthea
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004054585 | A1 | 20040701 | WO 2003-IB5826 | 20031208 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| US 2004254204 | A1 | 20041216 | US 2003-737691 | 20031216 |
| NL 1025044 | A1 | 20040621 | NL 2003-1025044 | 20031217 |

PRIORITY APPLN. INFO.: US 2002-434486P P 20021218
OTHER SOURCE(S): MARPAT 141:89096
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

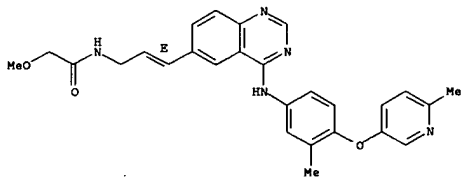
AB The invention relates to a preparation of 4-anilinoquinazoline derivs. of formula I [wherein: R1 is H or alkyl; R2 is H, alkyl, alkoxy, or hydroxyalkyl; R3 is H, alkyl, hydroxyalkyl, and CO2H, etc.; R4 is CO2H, CH2NHC(O)CH2OMe, or CH2NH2, etc.], useful for the treatment of abnormal cell growth. The invention also relates to methods of treating abnormal cell growth in mammals by administering the compds. of formula I. The prepared title compds. have IC50 values of < 10 μM against erbB2 kinase. For instance, (hydroxymethyl)anilinoquinazoline derivative II (R5 = CH2OH) was prepared via microbial biotransformation of methylanilinoquinazoline derivative II (R5 = Me) using Streptomyces albulus (example 2).

IT **383432-38-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed; preparation of anilinoquinazoline derivs. via microbial biotransformation)

RN 383432-38-0 CAPLUS
CN Acetamide, 2-methoxy-N-[(2E)-3-[4-[[3-methyl-4-[(6-methyl-3-pyridinyl)oxy]phenyl]amino]-6-quinazolinyl]-2-propenyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 16 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:453176 CAPLUS
DOCUMENT NUMBER: 141:7132
TITLE: Preparation of cyanoguanidine quinazoline and cyanoamidine quinazolamine derivatives as ErbB2 and EGFR inhibitors
INVENTOR(S): Wallace, Eli; Topalov, George; Zhao, Qian
PATENT ASSIGNEE(S): Array Biopharma, Inc., USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004046101 | A2 | 20040603 | WO 2003-US35670 | 20031110 |
| WO 2004046101 | A3 | 20040916 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-427544P P 20021120
OTHER SOURCE(S): MARPAT 141:7132
GI

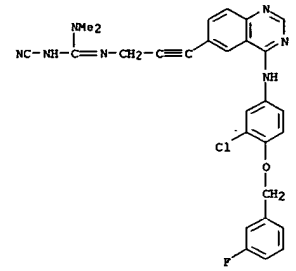
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein one of the positions 6 or 7 of the quinazoline ring must be substituted by A, and the remaining positions optionally substituted by R2; X = N, CH, C-CN; R1 = independently hetero/aryl substituted by at least one R6 and optionally substituted by up to three R5 groups; R5 = CN, Cl, F, Br, lower alkyl, CF3, CHF2, NO2, OH and derivs.; R6 = H, CN, Cl, F, Br, CF3, CHF2, OCF3, NO2, (un)substituted cycloalkyl/aryl/heteroaryl/cyclo/heterocyclyl/alkyl, hetero/aryl, alkenyl, alkynyl, heterocyclyl; A = -(T)m-L(D)-C(:N-CN)Q; T = (un)substituted cycloalkyl/aryl/heteroaryl/cyclo/heterocyclyl/alkyl, hetero/aryl, alkenyl, alkynyl, heterocyclyl; m = 0-1; L = N, CH, CF3, (un)substituted alk(en/yn)yl, hetero/aryl, etc.; Q = CH3 and derivs. with provisos; D = H, CF3, CHF2, SO2NH2 and derivs., CO2H and derivs., CONH2 and derivs., (un)substituted alk(en/yn)yl, hetero/aryl, etc.; their enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts and prodrugs] were prepared as ErbB2 and EGFR inhibitors for treating **proliferative** diseases. Alkylation of 3-chloro-4-(3-fluorobenzyloxy)phenylamine (preparation given) with 4-chloro-6-iodoquinazoline (preparation given), Pd-cross coupling of the iodide with (prop-2-ynyl)carbamic acid tert-Bu ester, and BOC-deprotection gave the amine II. Condensation

L5 ANSWER 17 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
of amine II with di-Ph cyanocarbonimidate, and reaction with NHMe2 gave the quinazoline cyanoguanidine III. Selected I modulated ErbB kinase activity with IC50 values in the range of 8-33 nM. I are useful for treating **cancer** and inflammation.

IT **697299-71-1P**, N-[3-[4-[[3-Chloro-4-(3-fluorobenzyloxy)phenyl]amino]quinazolin-6-yl]prop-2-ynyl]-N'-cyano-N'',N''-dimethylguanidine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU** (**Therapeutic use**); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinazolinylcyanoguanidines and quinazolaminocyanoamidines as ErbB2 and EGFR inhibitors)

RN 697299-71-1 CAPLUS
CN Guanidine, N'-[3-[4-[[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]amino]-6-quinazolinyl]-2-propynyl]-N''-cyano-N,N-dimethyl- (9CI) (CA INDEX NAME)

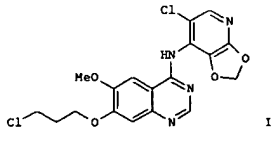


L5 ANSWER 18 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:430753 CAPLUS
DOCUMENT NUMBER: 141:1220
TITLE: Preparation of quinazolines as Src family non-receptor tyrosine kinase inhibitors for use in combination therapy with gemcitabine for treatment and prophylaxis of pancreatic **cancer**
INVENTOR(S): Barge, Alan
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004043472 | A1 | 20040527 | WO 2003-GB4787 | 20031107 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-26434 A 20021113
GI



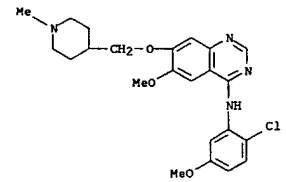
I

AB The invention concerns a combination comprising an inhibitor of Src kinase and the cytotoxic agent, gemcitabine, a pharmaceutical composition comprising such a combination, and its use in the treatment or prophylaxis of **cancer**, particularly of pancreatic **cancer**. Examples include prepns. for anilino- and (pyridylamino)quinazoline Src inhibitors (no Markush structure given) and bioassays demonstrating the synergistic effect of treating pancreatic **cancer** with a quinazoline Src inhibitor in combination with gemcitabine. For instance, 4-amino-5-chloro-2,3-methylenedioxypyridine was coupled with 4-chloro-7-(3-chloropropoxy)-6-methoxyquinazoline (preparation of reactants given) in the presence of sodium hexamethyldisilazane in THF to afford the (pyridylamino)quinazoline I. Nude mice were injected with pancreatic **tumor** cells derived from the COLO 357 human pancreatic **cancer** cell line and treated with gemcitabine, the Src inhibitor,

L5 ANSWER 18 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
4-(2-chloro-5-methoxyanilino)-6-methoxy-7-(N-methylpiperidin-4-ylmethoxy)quinazoline, or a combination of the two. Evaluation for **tumor** growth and incidence of liver metastases showed that, compared with the wt. of control tumors, **tumor** growth in animals treated with the combination was much reduced (1359 mg and 124 mg, resp.) to a level well below that achievable on the dosing of either gemcitabine or the Src inhibitor alone. In addn., there was no liver metastasis in the animals treated with the combination, whereas liver metastasis was present in 1/5 of the animals treated with gemcitabine alone.

IT **476159-98-5P**, 4-(2-Chloro-5-methoxyanilino)-6-methoxy-7-[(N-methylpiperidin-4-yl)methoxy]quinazoline
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU** (**Therapeutic use**); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor agent; preparation of quinazoline-containing Src inhibitors for use in synergistic combination with gemcitabine for treatment and prophylaxis of pancreatic **cancer**)

RN 476159-98-5 CAPLUS
CN 4-Quinazolinamine, N-(2-chloro-5-methoxyphenyl)-6-methoxy-7-[(1-methyl-4-piperidinyl)methoxy]- (9CI) (CA INDEX NAME)

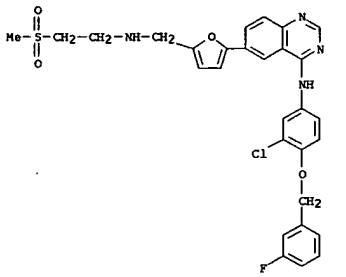


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 19 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:336121 CAPLUS
DOCUMENT NUMBER: 140:399538
TITLE: Inhibition of ErbB1 and ErbB2 by lapatinib ditosylate, a dual kinase inhibitor: Promising activity in pretreated advanced breast cancer
AUTHOR(S): Maung, Kavita; O'Shaughnessy, Joyce A.
CORPORATE SOURCE: USA
SOURCE: Clinical Breast Cancer (2004), 4(6), 398-400
CODEN: CBCLB7; ISSN: 1526-8209
PUBLISHER: Cancer Information Group, LP
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This article discusses the efficacy of lapatinib ditosylate, an inhibitor of the ErbB1 and ErbB2 kinase in patients with advanced breast cancer.
IT 388082-77-7, Lapatinib ditosylate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy of lapatinib ditosylate in pretreated advanced breast cancer)
RN 388082-77-7 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-, bis(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

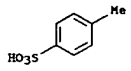
CM 1

CRN 231277-92-2
CMF C29 H26 Cl F N4 O4 S



CM 2

L5 ANSWER 19 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
CRN 104-15-4
CMF C7 H8 O3 S



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 20 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:200102 CAPLUS
DOCUMENT NUMBER: 140:235750
TITLE: Preparation of quinazolines as epidermal growth factor receptor (erbB) inhibitors for the treatment of proliferative diseases
INVENTOR(S): Kath, John Charles; Tom, Norma Jacqueline; Cox, Eric David; Bhattacharya, Samit Kumar
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

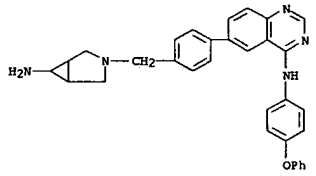
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 1396489 | A1 | 20040310 | EP 2003-24331 | 19991224 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY | | | | |
| EP 1029853 | A1 | 20000823 | EP 1999-310574 | 19991224 |
| EP 1029853 | B1 | 20040225 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| US 2003055049 | A1 | 20030320 | US 2002-226255 | 20020822 |
| PRIORITY APPLN. INFO.: | | | US 1999-117341P | P 19990127 |
| | | | EP 1999-310574 | A3 19991224 |
| | | | US 2000-488378 | A3 20000120 |

GI

I

AB Title compds. I [X = N, CH; A-B = R4-substituted fused pyridyl, pyrimidyl, furanyl, etc.; Y = NR1R3; R1, R2 = H, alkyl; R3 = -(CR1R2)m-R8 or R1 and R3 are taken together with N; R4 = -(CR1R2)p-aryl, -(CR1R2)p-heterocyclic, -(CR1R2)q-NR1R9, etc.; R8 = -(CR1R2)p-aryl, -(CR1R2)p-heterocyclic; R9 = fused or bridged bicyclic ring, spirocyclic ring with provisos; m= 0, 1; p, q = 0-5] and their pharmaceutically acceptable salts were prepared For example, coupling of compound I [X = N; A-B = -CR4=CH-CH=CH-; Y = OPh; R4 = 4-((6-hydroxymethyl-3-aza-bicyclo[3.1.0]hex-3-yl)methyl)phenyl], e.g., prepared from 6-iodo-4-quinazolinone in 4-steps, with 1-cyclopropylmethyl-1H-indol-5-ylamine, afforded compound I [X = N; A-B = -CR4=CH-CH=CH-; Y = 1-cyclopropylmethyl-1H-indol-5-ylamino; R4 = 4-((6-hydroxymethyl-3-aza-bicyclo[3.1.0]hex-3-yl)methyl)phenyl] in 67% yield. In c-erbB2 kinase inhibition assays, compds. I showed potent (sic.) inhibition of the erbB2 tyrosine kinase activity (no data provided). Compds. I are claimed useful for the treatment of cancer and benign proliferative diseases, e.g., psoriasis.
IT 289036-76-6P, [6-[4-(6-Amino-3-azabicyclo[3.1.0]hex-3-ylmethyl)phenyl]-quinazolin-4-yl][4-phenoxyphenyl]amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

L5 ANSWER 20 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
(Uses)
(prepn. of quinazolines as erbB inhibitors for the treatment of proliferative diseases)
RN 289036-76-6 CAPLUS
CN 3-Azabicyclo[3.1.0]hexan-6-amine, 3-[[4-[4-[(4-phenoxyphenyl)amino]-6-quinazolinyl]phenyl]methyl]- (9CI) (CA INDEX NAME)



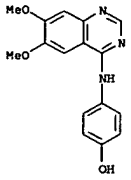
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 21 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:187250 CAPLUS
DOCUMENT NUMBER: 140:332000
TITLE: IL-7-dependent human leukemia T-cell line as a valuable tool for drug discovery in T-ALL
AUTHOR(S): Barata, Joao T.; Boussiotis, Vassiliki A.; Yunes, Jose A.; Ferrando, Adolfo A.; Moreau, Lisa A.; Veiga, J. Pedro; Sallan, Stephen E.; Look, A. Thomas; Nadler, Lee M.; Cardoso, Angelo A.
CORPORATE SOURCE: Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA
SOURCE: Blood (2004), 103(5), 1891-1900
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The specific targeting of critical signaling mols. may provide efficient therapies for T-cell acute lymphoblastic leukemia (T-ALL). However, target identification and drug development are limited by insufficient nos. of primary T-ALL cells and by their high rate of spontaneous apoptosis. The authors established a human interleukin-7 (IL-7)-dependent T-ALL cell line, TAIL7, that maintains several biol. and signaling properties of its parental leukemia cells. TAIL7 cells are pre-T-ALL cells that proliferate in response to IL-7 and IL-4. IL-7 stimulation of TAIL7 cells prevents spontaneous in vitro apoptosis and induces cell activation and cell cycle progression. The signaling events triggered by IL-7 include down-regulation of p27kip1 and hyperphosphorylation of retinoblastoma protein (Rb). Stimulation of TAIL7 cells by IL-7 leads to phosphorylation of Janus kinase 3 (JAK3), signal transducer and activator of transcription 5 (STAT5), Akt/PKB (protein kinase B), and extracellular-regulated kinase 1 and 2 (Erk1/2). Importantly, specific blockade of JAK3 by its inhibitor WHI-P131 abrogates the IL-7-mediated proliferation and survival of TAIL7 cells, suggesting that activation of JAK3 is critical for IL-7 responsiveness by these cells. Because TAIL7 cells seem to be a biol. surrogate for primary leukemia T cells, this cell line constitutes a valuable tool for the study of the signaling pathways implicated in T-ALL. Exploitation of this cell line should allow the identification of mol. targets and promote the rational design and validation of antileukemia signaling inhibitors.

IT **202475-60-3**, WHI-P131
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(interleukin 7-dependent human leukemia T-cell line as a valuable tool for drug discovery in T cell acute lymphoblastic leukemia in relation to signaling pathways as drug targets)
RN 202475-60-3 CAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 21 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

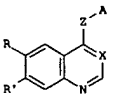


REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 22 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:182845 CAPLUS
DOCUMENT NUMBER: 140:217519
TITLE: Preparation of quinoline derivatives as TGFβ inhibitors
INVENTOR(S): Shimizu, Kiyoshi; Shimizu, Toshiyuki; Kimura, Kaname; Kawakami, Kazuki; Nakoji, Masayoshi
PATENT ASSIGNEE(S): Kirin Beer Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 628 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004018430 | A1 | 20040304 | WO 2003-JP10647 | 20030822 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

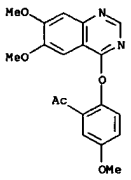
PRIORITY APPLN. INFO.: JP 2002-244029 A 20020823
OTHER SOURCE(S): MARPAT 140:217519
GI



AB The title compds. I [wherein X = CH or N; Z = O, NH, S, or CO; R and R' = independently H, halo, (un)substituted alkyl, alkenyl, NH2, CONH2, OH, or heterocyclyl; A = (un)substituted Ph or (hetero)cyclyl] or pharmaceutically acceptable salts, or solvates thereof are prepared as transforming growth factor (TGF) β inhibitors. For example, 4-chloro-6,7-dimethoxyquinoline was reacted with 2-benzylphenol in 1,2-dichlorobenzene to give 4-(2-benzylphenoxy)-6,7-dimethoxyquinoline (10%). Some of compds. I inhibited 100% of human TGFβ at 10 μM.

IT **666730-78-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinoline derivs. as TGFβ inhibitors)
RN 666730-78-5 CAPLUS
CN Ethanone, 1-[2-[(6,7-dimethoxy-4-quinazolinyl)oxy]-5-methoxyphenyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 22 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



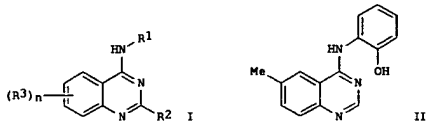
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 23 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:120821 CAPLUS
DOCUMENT NUMBER: 140:163886
TITLE: Preparation of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases
INVENTOR(S): Gazit, Aviv; Levitzki, Alexander
PATENT ASSIGNEE(S): Yissum Research Development Company of the Hebrew University of Jerusalem, Israel
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004013091 | A2 | 20040212 | WO 2003-IL632 | 20030731 |
| WO 2004013091 | A3 | 20040729 | | |

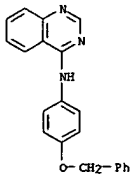
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-399736P P 20020801
OTHER SOURCE(S): MARPAT 140:163886
GI




AB Title compds. I [R1 = (un)substituted Ph, naphthyl, etc.; R2 = H, halo, phenylamino, etc.; R3 = H, alkoxy, NO2, etc.; n = 1-3] are prepared For instance, 4-chloro-6-methylquinazoline is reacted with 2-aminophenol (EtOH, reflux, 1 h) to give II. I are potent inhibitors of protein tyrosine (PTK) kinase activity, particularly epidermal growth factor receptor (EGFR) kinase activity. I are useful in treating a variety of PTK related disorders such as cell **proliferative** disorders, fibrotic disorders, metabolic disorders and **cancer**.
IT **77725-90-7P**, 4-[[4-[Benzyloxy]phenyl]amino]quinazoline

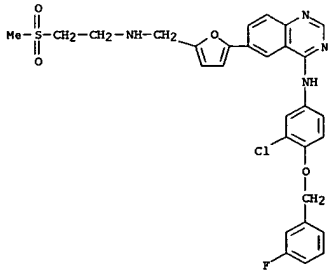
L5 ANSWER 23 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases)
RN 77725-90-7 CAPLUS
CN 4-Quinazolinamine, N-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)




L5 ANSWER 24 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:108301 CAPLUS
DOCUMENT NUMBER: 141:199241
TITLE: Emerging role of epidermal growth factor receptor inhibition in therapy for advanced malignancy: focus on NSCLC
AUTHOR(S): Langer, Corey J.
CORPORATE SOURCE: Department of Thoracic Oncology, Fox Chase Cancer Center, Philadelphia, PA, 19111, USA
SOURCE: International Journal of Radiation Oncology, Biology, Physics (2004), 58(3), 991-1002
CODEN: IOBPD3; ISSN: 0360-3016
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Combination chemotherapy regimens have emerged as the standard approach in advanced non-small-cell lung **cancer**. Meta-analyses have demonstrated a 2-mo increase in median survival after platinum-based therapy vs. best supportive care, and an absolute 10% improvement in the 1-yr survival rate. Just as importantly, cytotoxic therapy has produced benefits in symptom control and quality of life. Newer agents, including the taxanes, vinorelbine, gemcitabine, and irinotecan, have expanded our therapeutic options in the treatment of advanced non-small-cell lung **cancer**. Despite their contributions, we have reached a therapeutic plateau, with response rates seldom exceeding 30-40% in cooperative group studies and 1-yr survival rates stable between 30% and 40%. It is doubtful that substituting one agent for another in various combinations will lead to any further improvement in these rates. The thrust of current research has focused on targeted therapy, and epidermal growth factor receptor inhibition is one of the most promising clin. strategies. Epidermal growth factor receptor inhibitors currently under investigation include the small mols. gefitinib (Iressa, ZD1839) and erlotinib (Tarceva, OSI-774), as well as monoclonal antibodies such as cetuximab (IMC-225, Erbitux). Agents that have only begun to undergo clin. evaluation include CI-1033, an irreversible pan-erbB tyrosine kinase inhibitor, and PKI166 and GW572016, both examples of dual kinase inhibitors (inhibiting epidermal growth factor receptor and Her2). Preclin. models have demonstrated synergy for all these agents in combination with either chemotherapy or radiotherapy, leading to great enthusiasm regarding their ultimate contribution to lung **cancer** therapy. However, serious clin. challenges persist. These include the identification of the optimal dose(s); the proper integration of these agents into popular, established cytotoxic regimens; and the selection of the optimal setting(s) in which to test these compds. Both gefitinib and erlotinib have shown clin. activity in pretreated, advanced non-small-cell lung **cancer**, but placebo-controlled randomized Phase III studies evaluating gefitinib in combination with standard cytotoxic therapy, to our chagrin, have failed to demonstrate a survival advantage compared with chemotherapy alone.
IT **231277-92-2**, GW572016
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(Emerging role of epidermal growth factor receptor inhibition in therapy for nonsmall-cell-lung **cancer** patients)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 24 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)




REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 25 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:100947 CAPLUS
DOCUMENT NUMBER: 140:139486
TITLE: Method of treating **cancer**
INVENTOR(S): Potter, David A.
PATENT ASSIGNEE(S): Advanced Research & Technology Institute at Indiana University, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004010937 | A2 | 20040205 | WO 2003-US23437 | 20030728 |
| WO 2004010937 | A3 | 20040527 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004167139 | A1 | 20040826 | US 2003-629045 | 20030728 |

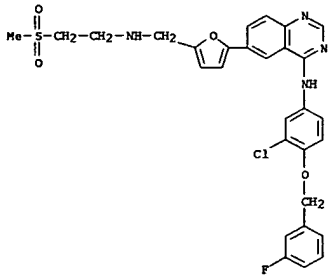
PRIORITY APPLN. INFO.: US 2002-399573P P 20020726

AB Methods for treating **cancer** are described here. The methods include administering to an HIV-neg. patient an m-calpain inhibitor such as ritonavir. Ritonavir or other m-calpain inhibitors can also be co-administered with other therapeutic agents such as a Cox-2 inhibitor, a taxane, or a proteasome inhibitor. Methods for determining whether a patient will respond to a particular method of treatment are also described herein.

IT **231277-92-2**, GW 572016
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(treating **cancer**)

RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 25 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



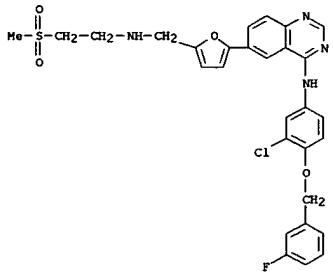
L5 ANSWER 26 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:78650 CAPLUS
DOCUMENT NUMBER: 141:291328
TITLE: Effects of the EGFR/HER2 kinase inhibitor GW572016 on EGFR- and HER2-overexpressing breast **cancer** cell line **proliferation**, radiosensitization, and resistance
AUTHOR(S): Zhou, Hong; Kim, Yeon-Shil; Peletier, Aaron; McCall, Wes; Earp, H. Shelton; Sartor, Carolyn I.
CORPORATE SOURCE: Department of Radiation Oncology, University of North Carolina School of Medicine and UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC, 27599, USA
SOURCE: International Journal of Radiation Oncology, Biology, Physics (2004), 58(2), 344-352
CODEN: IOBPD3; ISSN: 0360-3016
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: Two members of the epidermal growth factor receptor family, EGFR and HER2, have been implicated in radioresistance in breast **cancer** and other malignancies. To gauge the potential clin. utility of targeting both EGFR and HER2 to control growth and radiosensitize human breast cancers, we examined the effect of a dual EGFR/HER2 inhibitor, GW572016, on the **proliferation** and radiation response of either EGFR- or HER2-overexpressing human breast **cancer** cell lines. Methods and materials: Primary human breast **cancer** cell lines that endogenously overexpress EGFR or HER2 and luminal mammary epithelial H16N2 cells stably transfected with HER2 were evaluated for the effect of GW572016 on inhibition of ligand-induced or constitutive receptor phosphorylation, **proliferation**, radiosensitization, and inhibition of downstream signaling. Results: GW572016 inhibited constitutive and/or ligand-induced EGFR or HER2 tyrosine phosphorylation of all five cell lines, which correlated with the antiproliferative response in all but one cell line. GW572016 radiosensitized EGFR-overexpressing cell lines, but HER2-overexpressing cells were unable to form colonies after brief exposure to GW572016 even in the absence of radiation, and thus could not be evaluated for radiosensitization. One cell line was resistant to the antiproliferative and radiosensitizing effects of GW572016, despite receptor inhibition. Exploration of potential mechanisms of resistance in SUM185 cells revealed failure of GW572016 to inhibit downstream ERK and Akt activation, despite inhibition of HER2 phosphorylation. In contrast, sensitive HER2-overexpressing cell lines demonstrated inhibition of both ERK and Akt phosphorylation. Conclusion: GW572016 potently inhibits receptor phosphorylation in either EGFR- or HER2-overexpressing cell lines and has both antiproliferative and radiosensitizing effects. Resistance to GW572016 was not due to a lack of receptor inhibition, but rather with a lack of inhibition of ERK and Akt, suggesting that measurement of inhibition of crucial signaling pathways may better predict response than inhibition of receptor phosphorylation. The SUM185 cell line provides a valuable model for studying mechanisms of resistance of EGFR/HER2 inhibitor therapy.

IT **231277-92-2**, GW572016
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(effects of EGFR/HER2 kinase inhibitor GW572016 on EGFR- and HER2-overexpressing breast **cancer** cell line **proliferation**, radiosensitization, and resistance)

RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 26 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 27 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:60252 CAPLUS
DOCUMENT NUMBER: 140:128427
TITLE: Preparation of quinazolines as ephrin and EGFR receptor kinase modulators for treating cancer and other disorders
INVENTOR(S): Rice, Kenneth D.; Anand, Neel Kumar; Bussenius, Joerg; Costanzo, Simona; Kennedy, Abigail R.; Kim, Angie I.; Peto, Csaba J.; Tsang, Tsze H.; Blazey, Charles M.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 266 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004006846 | A2 | 20040122 | WO 2003-US21923 | 20030714 |
| WO 2004006846 | A3 | 20040715 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

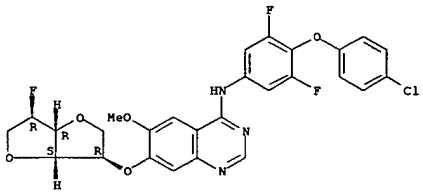
PRIORITY APPLN. INFO.: US 2002-396269P P 20020715
US 2003-447212P P 20030213
OTHER SOURCE(S): MARPAT 140:128427
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

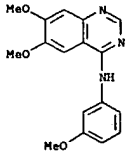
AB The present invention provides quinazolines (shown as I; variables defined below; e.g. II and III) for modulating receptor tyrosine kinase activity, particularly ephrin and EGFR, and methods of treating diseases mediated by receptor kinase activity using the compds. and pharmaceutical compns. thereof. Diseases mediated by receptor kinase activity include, but are not limited to, diseases characterized in part by abnormal levels of cell **proliferation** (i.e. **tumor** growth), programmed cell death (apoptosis), cell migration and invasion and angiogenesis associated with **tumor** growth. Compds. of the invention include 'spectrum selective' kinase modulators, compds. that inhibit, regulate and/or modulate signal transduction across subfamilies of receptor-type tyrosine kinases, including ephrin and EGFR. Inhibitory activities for >200 examples of I are tabulated for some or all of EphB4, EphA2, KDR, Flt-1, EGFR and ErbB2 kinases. Although the methods of preparation are not claimed, 37 example prepns. are included. For example, 1,4:3,6-dianhydro-2-O-[4-[(3-chloro-2-methylphenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-

L5 ANSWER 27 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
L-iditol hydrochloride was prepd. in 2 steps (94, 51 % yields, resp.) starting with mesylation of 1,4:3,6-dianhydro-2-O-methyl-D-glucitol followed by ether formation of the intermediate 1,4:3,6-dianhydro-2-O-methyl-5-O-(methylsulfonyl)-D-glucitol with 4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-ol; the quinazolinol was prepd. in 64 % yield from 4-chloro-6-(methyloxy)-7-[(phenylmethyl)oxy]quinazoline hydrochloride and 3,4-dichloroaniline. For I: R1 is C1-C3 (un)substituted alkyl; R2 = H, halogen, trihalomethyl, CN, NH2, NO2, OR3, N(R3)R4, S(O)0-2R4, SO2N(R3)R4, CO2R3, C(O)N(R3)R4, N(R3)SO2R4, N(R3)C(O)R3, N(R3)CO2R4, C(O)R3, (un)substituted lower alkyl, (un)substituted lower alkenyl, and (un)substituted lower alkynyl; R3 is H or R4; R4 = (un)substituted lower alkyl, (un)substituted aryl, (un)substituted lower arylalkyl, (un)substituted heterocyclyl, and (un)substituted lower heterocyclylalkyl; or R3 and R4, when taken together with a common N to which they are attached, form an (un)substituted 5-7-membered heterocyclyl, said (un)substituted five-to seven-membered heterocyclyl optionally contg. at least one addnl. heteroatom = N, O, S, and P. Q is O-5; Z = OCH2, O, S(O)0-2, N(R5)CH2, and NR5; R5 is -H or (un)substituted lower alkyl; M1 is H, (un)substituted C1-C8 alkyl-L2-L1, G(CH2)0-3, or R53(R54)N(CH2)0-3; wherein G is a satd. 5-7-membered heterocyclyl contg. 1-2 annular heteroatoms; L1 is C:O or SO2; L2 is a direct bond, O, or NH; M2 is a satd. or mono- or polyunsatd. C3-C14 mono- or fused-polycyclic hydrocarbyl optionally contg. 1-3 annular heteroatoms per ring; M3 is NR9, O, or absent; M4 is CH2, CH2CH2, CH2CH2CH2, or absent; addnl. details are given in the claims.
IT **650579-00-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinazolines as ephrin and EGFR receptor kinase modulators for treating **cancer** and other disorders)
RN 650579-00-3 CAPLUS
CN D-Iditol, 1,4:3,6-dianhydro-5-O-[4-[[4-(4-chlorophenoxy)-3,5-difluorophenyl]amino]-6-methoxy-7-quinazolinyl]-2-deoxy-2-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 28 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:45404 CAPLUS
DOCUMENT NUMBER: 140:228458
TITLE: Discovery of a New Class of Anilinoquinazoline Inhibitors with High Affinity and Specificity for the Tyrosine Kinase Domain of c-Src
AUTHOR(S): Ple, Patrick A.; Green, Tim P.; Hennequin, Laurent F.; Curwen, Jon; Fennell, Michael; Allen, Jack; Lambert-van der Brempt, Christine; Costello, Gerard
CORPORATE SOURCE: Centre de Recherches, AstraZeneca, Reims, 51689, Fr.
SOURCE: Journal of Medicinal Chemistry (2004), 47(4), 871-887
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Deregulated activity of the nonreceptor tyrosine kinase c-Src is believed to result in signal transduction, cytoskeletal and adhesion changes, ultimately promoting a **tumor**-invasive phenotype. We report here the discovery of a new class of anilinoquinazoline inhibitors with high affinity and specificity for the tyrosine kinase domain of the c-Src enzyme. Special attention was directed toward finding inhibitors selective against KDR tyrosine kinase in order to ensure that the in vivo profile of a specific Src inhibitor could be determined The 4-aminobenzodioxole quinazoline series gave compds. with excellent potency and selectivity. The most interesting compds. were evaluated in vivo and displayed good pharmacokinetics following oral dosing. Compds. such as the aminobenzodioxoles were shown to be potent inhibitors of **tumor** growth in a c-Src-transformed 3T3 xenograft model in vivo, resulting in more than 90% growth inhibition at doses as low as 6 mg/kg po once daily. Src tyrosine kinase inhibitors such as these may provide a novel therapeutic modality for targeting **cancer** invasion and metastasis.
IT **202475-38-5P**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and structure-activity relationship of new class of anilinoquinazoline inhibitors with high affinity and specificity for tyrosine kinase domain of c-Src)
RN 202475-38-5 CAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-N-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

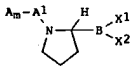
L5 ANSWER 28 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L5 ANSWER 29 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:41229 CAPLUS
DOCUMENT NUMBER: 140:105266
TITLE: Boroproline compound combination therapy for various diseases
INVENTOR(S): Adams, Sharlene; Miller, Glenn T.; Jesson, Michael I.; Jones, Barry
PATENT ASSIGNEE(S): Point Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004004661 | A2 | 20040115 | WO 2003-US21547 | 20030709 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004077601 | A1 | 20040422 | US 2003-616694 | 20030709 |

PRIORITY APPLN. INFO.:
US 2002-394856P P 20020709
US 2002-414978P P 20021001
US 2003-466435P P 20030428

GI

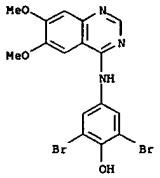


I

AB A method is provided for treating subjects with combination therapy including compds. of Formula I (wherein m is an integer between 0 and 10, inclusive; A and A1 may be L- or D-amino acid residues, the C bonded to B is in the L-configuration, and each X1 and X2 is, independently, a hydroxy group or a group capable of being hydrolyzed to a hydroxy group in aqueous solution at physiol. pH). It was surprisingly discovered that this combination enhanced the efficacy of both agents, and that administration of Formula I compds. induced cytokine and chemokine production in vivo. The combinations can be used to enhanced ADCC, stimulate immune responses and /or patient and treat certain disorders. The invention also relates to kits and compns. relating to such combinations.

IT 211555-05-4, WHI-P97
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

L5 ANSWER 29 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
(boroproline compd. combination therapy for various diseases)
RN 211555-05-4 CAPLUS
CN Phenol, 2,6-dibromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L5 ANSWER 30 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:41226 CAPLUS
DOCUMENT NUMBER: 140:105321
TITLE: Methods and compositions relating to isoleucine boroproline compounds
INVENTOR(S): Adams, Sharlene; Miller, Glenn T.; Jesson, Michael I.; Jones, Barry
PATENT ASSIGNEE(S): Point Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004004658 | A2 | 20040115 | WO 2003-US21405 | 20030709 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004077601 | A1 | 20040422 | US 2003-616694 | 20030709 |

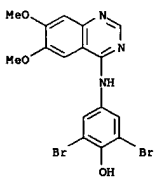
PRIORITY APPLN. INFO.:
US 2002-394856P P 20020709
US 2002-414978P P 20021001
US 2003-466435P P 20030428

OTHER SOURCE(S): MARPAT 140:105321

AB A method for treating subjects with, inter alia, abnormal cell proliferation or infectious disease using agents of formula (I, AmNHCH(CH(CH3)CH2CH3)COA1R) (where Am and A1 are amino acids and R = organo boronates, organo phosphonates, fluoroalkyl ketones, alphaketos, N-peptioyl-O-(acylhydroxylamines), azapeptides, azetidines, fluoroolefins dipeptide isosteres, peptidyl (α-aminoalkyl) phosphonate esters, aminoacyl pyrrolidine-2-nitriles and 4-cyanothiazolidides) is claimed. Methods for stimulating an immune response using the compds. of the invention are also claimed. Compns. containing Ile-boroPro compds. are also provided as are kits containing the compns. The invention embraces the use of these compds. alone or in combination with other therapeutic agents.

IT 211555-05-4, WHI-P97
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic methods and compns. relating to isoleucine boroproline compds. alone or in combination with other drugs, antibodies, or antigens)
RN 211555-05-4 CAPLUS
CN Phenol, 2,6-dibromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 30 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L5 ANSWER 31 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:20322 CAPLUS
DOCUMENT NUMBER: 140:87658
TITLE: Peptidomimetic modulators of cell adhesion
INVENTOR(S): Gour, Barbara J.; Blaschuk, Orest W.; Ali, Anmar; Ni, Feng; Chen, Zhigang; Michaud, Stephanie Denise; Wang, Shaomeng; Hu, Zengjian
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 280 pp., Cont.-in-part of U.S. Ser. No. 6,982.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004006011 | A1 | 20040108 | US 2003-425557 | 20030428 |
| US 6031072 | A | 20000229 | US 1997-893534 | 19970711 |
| US 6326352 | B1 | 20011204 | US 2000-507102 | 20000217 |
| US 2002168761 | A1 | 20021114 | US 2001-769145 | 20010124 |
| US 2002151475 | A1 | 20021017 | US 2001-6982 | 20011204 |

PRIORITY APPLN. INFO.:
US 1996-21612P P 19960712
US 1997-893534 A1 19970711
US 2000-491078 B2 20000124
US 2000-507102 A1 20000217
US 2001-769145 B2 20010124
US 2001-6982 A2 20011204

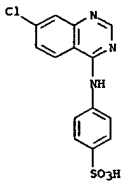
OTHER SOURCE(S): MARPAT 140:87658

AB Peptidomimetics of cyclic peptides, and compns. comprising such peptidomimetics are provided. The peptidomimetics have a three-dimensional structure that is substantially similar to a three-dimensional structure of a cyclic peptide that comprises a cadherin cell adhesion recognition sequence HAV. Methods for using such peptidomimetics for modulating cadherin-mediated cell adhesion in a variety of contexts are also provided.

IT **105037-36-3**, Benzenesulfonic acid, 4-[(7-chloro-4-quinazolinyl)amino]-
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(peptidomimetic modulators of cadherin-mediated cell adhesion for therapeutic use in relation to three-dimensional structure)

RN 105037-36-3 CAPLUS
CN Benzenesulfonic acid, 4-[(7-chloro-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 31 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L5 ANSWER 32 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:2613 CAPLUS
DOCUMENT NUMBER: 140:53400
TITLE: **Cancer** biomarker expression/activation-based method for predicting response to HER1/HER2-directed **cancer** therapy
INVENTOR(S): Bacus, Sarah S.
PATENT ASSIGNEE(S): Ventana Medical Systems, Inc., USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004000101 | A2 | 20031231 | WO 2003-US19697 | 20030619 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

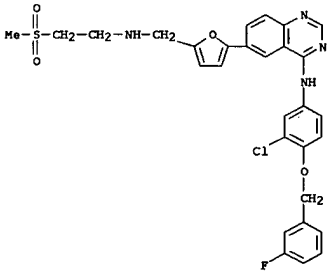
PRIORITY APPLN. INFO.:
US 2002-389795P P 20020619
US 2002-432811P P 20021211

AB This invention provides methods for determining or predicting response to HER1/HER2-directed **cancer** therapy in an individual. The methodol. of the invention includes assaying a **tumor** sample with one or more reagents that detect expression and/or activation of predictive biomarkers for **cancer**, e.g. growth factor receptors, growth factor receptor ligands, and growth factor receptor-related downstream signaling mols.

IT **231277-92-2**, GW572016
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**cancer** biomarker expression/activation-based method for predicting response to HER1/HER2-directed **cancer** therapy)

RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 32 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L5 ANSWER 33 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:2612 CAPLUS
DOCUMENT NUMBER: 140:53399
TITLE: Predictive markers in cancer therapy
INVENTOR(S): Bacus, Sarah S.; Herrle, Myra R.; Kirk, L. Edward; Spector, Neil L.; Stocum, Michael T.; Xia, Wenle
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

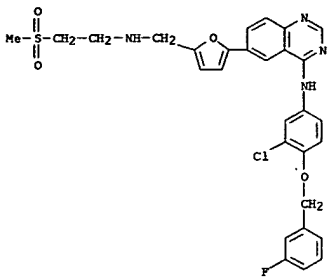
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004000094 | A2 | 20031231 | WO 2003-US12739 | 20030424 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 2002-389795P P 20020619
US 2002-432811P P 20021211
US 2002-432943P P 20021211
US 2003-451978P P 20030303

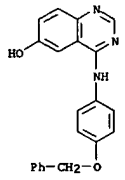
AB Mol. markers useful in medicine response tests are provided, as an aid in determining whether an individual subject's tumor is responding to treatment with EGF and/or erbB2 inhibitors. Markers include phosphorylated ERK protein.
IT **231277-92-2**, GW572016
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(predictive markers in cancer therapy)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 33 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L5 ANSWER 34 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:981459 CAPLUS
DOCUMENT NUMBER: 140:228690
TITLE: Synthesis and SAR of potent EGFR/erbB2 dual inhibitors
AUTHOR(S): Zhang, Yue-Mei; Cockerill, Stuart; Guntrip, Stephen B.; Rusnak, David; Smith, Kathryn; Vanderwall, Dana; Wood, Edgar; Lackey, Karen
CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(1), 111-114
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of 6-alkoxy-4-anilinoquinazoline compds. was prepared and evaluated for in vitro inhibition of the erbB2 and EGFR kinase activity. The IC50 values of the best compds. were below 0.10 uM. Further, several of these compds. inhibit the growth of erbB2 and EGFR over-expressing tumor cell lines at concns. below 1 uM.
IT **179246-81-2P**
RL: PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis and structure-activity relations of potent EGFR/erbB2 kinase dual inhibitors)
RN 179246-81-2 CAPLUS
CN 6-Quinazolinol, 4-[[4-(phenylmethoxy)phenyl]amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 35 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:971922 CAPLUS
DOCUMENT NUMBER: 140:23220
TITLE: Preventives and/or remedies for subjects with the expression or activation of her2 and/or EGFR
INVENTOR(S): Suzuki, Tsuyoshi; Kitano, Yasunori; Yano, Shinji
PATENT ASSIGNEE(S): Mitsubishi Pharma Corporation, Japan
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

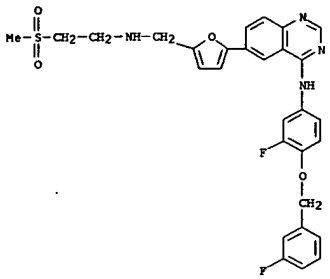
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003101491 | A1 | 20031211 | WO 2003-JP6988 | 20030603 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-162130 A 20020603
OTHER SOURCE(S): MARPAT 140:23220

AB Her2 and/or EGFR inhibitors to be administered to subjects with the overexpression or activation of Her2 and/or EGFR that have been subjected to an examination for detecting the expression or activity of Her2 and/or EGFR and thus regarded as having the overexpression or activation of Her and/or EGFR; and medicinal compns. containing such an inhibitor.
IT **231277-81-9**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(quinazoline analogs as preventives and/or remedies for subjects with the expression or activation of her2 and/or EGFR)
RN 231277-81-9 CAPLUS
CN 4-Quinazolinamine, N-[3-fluoro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 35 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 36 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

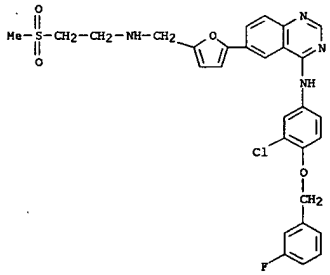
ACCESSION NUMBER: 2003:917646 CAPLUS
DOCUMENT NUMBER: 140:38051
TITLE: Epidermal Growth Factor Receptor Autocrine Signaling in RIE-1 Cells Transformed by the Ras Oncogene Enhances Radiation Resistance
AUTHOR(S): Grana, Theresa M.; Sartor, Carolyn I.; Cox, Adrienne D.
CORPORATE SOURCE: Curriculum in Genetics and Molecular Biology, Department of Radiation Oncology, University of North Carolina, Chapel Hill, NC, USA
SOURCE: Cancer Research (2003), 63(22), 7807-7814
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Oncogenic forms of the small GTPase Ras increase the resistance of cells to killing by ionizing radiation (IR). Although not all of the signaling pathways for radioresistance are well defined, it is now clear that Ras-dependent signaling pathways involved in radioresistance include those mediated by phosphatidylinositol 3'-kinase (PI3-K) and Raf. Nevertheless, PI3-K and Raf together are not sufficient to reconstitute all of the resistance conferred by Ras, indicating that other effectors must also contribute. We show here that Ras-driven autocrine signaling through the epidermal growth factor receptor (EGFR) also contributes to radioresistance in Ras-transformed cells. Conditioned media (CM) collected from RIE-1 rat intestinal epithelial cells expressing oncogenic Ras increased the survival of irradiated cells. Ras-CM contains elevated levels of the EGFR ligand transforming growth factor α (TGF-α). Both Ras-CM and TGF-α stimulated EGFR phosphorylation, and exogenous TGF-α mimicked the effects of Ras-CM to increase radioresistance. Blocking EGFR signaling with the EGFR/HER-2 kinase inhibitor (KI) GW572016 decreased the postradiation survival of irradiated Ras-transformed cells and normal cells but had no effect on the survival of unirradiated cells. Ras-CM and TGF-α also increase PI3-K activity downstream of the EGFR and increase postradiation survival, both of which are abrogated by GW572016. Thus, Ras utilizes autocrine signaling through EGFR to increase radioresistance, and the EGFR KI GW572016 acts as a radiosensitizer. The observation that Ras-transformed cells can be sensitized to killing by ionizing radiation with GW572016 demonstrates that EGFR KIs could potentially be used to radiosensitize tumors in which radioresistance is dependent on Ras-driven autocrine signaling through EGFR.

IT **231277-92-2**, GW572016
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(Ras utilizes autocrine signaling through EGF receptor to increase radioresistance in Ras-transformed cells and GW572016 acts as a radiosensitizer)

RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 36 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

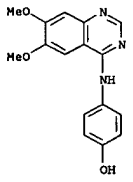
L5 ANSWER 37 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:849528 CAPLUS
DOCUMENT NUMBER: 140:174738
TITLE: Prevention of islet allograft rejection in diabetic mice by targeting janus kinase 3 with 4-(4'-hydroxyphenyl)-amino-6,7-dimethoxyquinazoline (JANEX-1)
AUTHOR(S): Cetkovic-Cvrlje, Marina; Dragt, Angela L.; Uckun, Fatih M.
CORPORATE SOURCE: Department of Immunology, Parker Hughes Institute and Parker Hughes Cancer Center, St. Paul, MN, USA
SOURCE: Arzneimittel-Forschung (2003), 53(9), 648-654
CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER: Editio Cantor Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Janus kinase (JAK) 3-deficient mice were not able to reject allogeneic islet allografts. The JAK3 inhibitor 4-(4'-hydroxyphenyl)-amino-6,7-dimethoxyquinazoline (CAS 202475-60-3, JANEX-1, WHIP131) prevented the rejection of islet allografts in mice with a normal JAK3 expression status. The combination of JANEX-1 and cyclosporin A (CAS 59865-13-3) was more effective than either agent alone.

IT **202475-60-3**, JANEX-1
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(prevention of islet allograft rejection in diabetic mice by targeting janus kinase 3 with 4-(4'-hydroxyphenyl)-amino-6,7-dimethoxyquinazoline (JANEX-1))

RN 202475-60-3 CAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

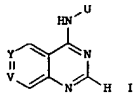


REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 38 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:836903 CAPLUS
DOCUMENT NUMBER: 139:317433
TITLE: **Cancer** treatment method comprising administering an erb-family inhibitor and a raf and/or ras inhibitor
INVENTOR(S): Spector, Neil Lee; Xia, Wenle
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

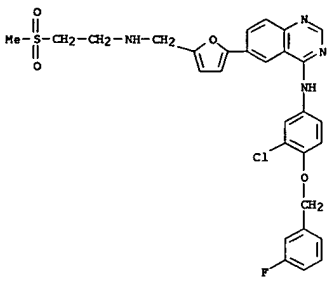
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003086467 | A1 | 20031023 | WO 2003-US10747 | 20030408 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1492568 | A1 | 20050105 | EP 2003-718262 | 20030408 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |

PRIORITY APPLN. INFO.: US 2002-370807P P 20020408
WO 2003-US10747 W 20030408
OTHER SOURCE(S): MARPAT 139:317433
GI



AB The invention provides a method for treating **cancer** in a mammal, as well as pharmaceutical combinations useful in such treatment. In particular, the method relates to a **cancer** treatment method that includes administering an erb family inhibitor and a Raf and/or ras inhibitor to a mammal suffering from a **cancer**. Preparation of compds., e.g. erbB-2/EGFR inhibitor I, is described.
IT **231277-92-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU**

L5 ANSWER 38 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
**(Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(erb-family inhibitor and raf and/or ras inhibitor combination for **cancer** treatment)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

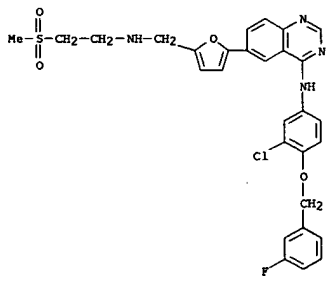


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 39 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:818866 CAPLUS
DOCUMENT NUMBER: 140:104
TITLE: Lapatinib ditosylate (GlaxoSmithKline
AUTHOR(S): Kim, Tracy E.; Murren, John R.
CORPORATE SOURCE: Beverly Hills, CA, 90211, USA
SOURCE: IDrugs (2003), 6(9), 886-893
CODEN: IDRUFN; ISSN: 1369-7056
PUBLISHER: Current Drugs
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Lapatinib ditosylate, an ErbB-2 and EGFR dual tyrosine kinase inhibitor, is being developed by GlaxoSmithKline plc for the potential treatment of solid tumors.
IT **388082-77-7**, Lapatinib ditosylate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(lapatinib ditosylate for potential treatment of solid tumors)
RN 388082-77-7 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-, bis(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

CM 1

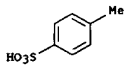
CRN 231277-92-2
CMF C29 H26 Cl F N4 O4 S



CM 2

CRN 104-15-4
CMF C7 H8 O3 S

L5 ANSWER 39 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



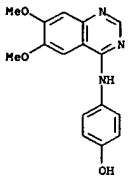
REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 40 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:633416 CAPLUS
DOCUMENT NUMBER: 139:173786
TITLE: Method for treating diseases associated with abnormal kinase activity
INVENTOR(S): Lyons, John; Rubinfeld, Joseph
PATENT ASSIGNEE(S): Supergen, Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003065995 | A2 | 20030814 | WO 2003-US3537 | 20030206 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2003147813 | A1 | 20030807 | US 2002-71849 | 20020207 |
| US 2004127453 | A1 | 20040701 | US 2002-206854 | 20020726 |
| PRIORITY APPLN. INFO.: | | | US 2002-71849 | A1 20020207 |
| | | | US 2002-206854 | A1 20020726 |

AB Methods are provided for treating diseases associated with abnormal activity of kinases such as chronic myelogenous leukemia. The method comprises: administering a DNA methylation inhibitor to the patient in therapeutically effective amount; and administering a kinase inhibitor such as imatinib mesylate to the patient in therapeutically effective amount, such that the in vivo activity of the kinase is reduced relative to that prior to the treatment. The method can be used to treat cancer associated with abnormal activity of kinases such as phosphatidylinositol 3'-kinase (P13K), protein kinases including serine/threonine kinases such as Raf kinases, protein kinase kinases such as MEK, and tyrosine kinases such as those in the epidermal growth factor receptor family (EGFR), platelet-derived growth factor receptor family (PDGFR), vascular endothelial growth factor receptor (VEGFR) family, nerve growth factor receptor family (NGFR), fibroblast growth factor receptor family (FGFR) insulin receptor family, ephrin receptor family, Met family, Ror family, c-kit family, Src family, Fes family, JAK family, Fak family, Btk family, Syk/ZAP-70 family, and Abl family.
IT 202475-60-3, 4-(4'-Hydroxyphenyl)amino-6,7-dimethoxyquinazoline
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of diseases associated with abnormal tyrosine kinase activity with tyrosine kinase inhibitor and DNA methylation inhibitor)
RN 202475-60-3 CAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 40 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

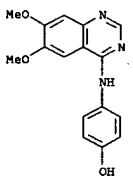


L5 ANSWER 41 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN.
ACCESSION NUMBER: 2003:633389 CAPLUS
DOCUMENT NUMBER: 139:159929
TITLE: Non-myeloablative tolerogenic treatment with tyrphostins
INVENTOR(S): Slavin, Shimon; Morecki, Shoshana; Levitzki, Alexander; Gazit, Aviv
PATENT ASSIGNEE(S): Yissum Research Development Company of the Hebrew University of Jerusalem, Israel; Hadasit Medical Research Services and Development Ltd.
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003065971 | A2 | 20030814 | WO 2002-IL467 | 20020616 |
| WO 2003065971 | C2 | 20031120 | | |
| WO 2003065971 | A3 | 20040916 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1482983 | A2 | 20041208 | EP 2002-738590 | 20020616 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2004197335 | A1 | 20041007 | US 2003-479523 | 20031211 |
| PRIORITY APPLN. INFO.: | | | US 2001-297795P | P 20010614 |
| | | | WO 2002-IL467 | W 20020616 |

AB A method of inducing immune tolerance in a first mammal to antigens of a second, non-syngeneic, mammal, is disclosed. The method is utilized to minimize graft rejection and/or reduce graft-vs.-host diseases in transplantation procedures and to produce hematopoietic mixed chimeras. Methods of determining the activity of tyrphostins and the optimal concentration thereof in this method are also disclosed.
IT 202475-60-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(non-myeloablative tolerogenic treatment with tyrphostins to eliminate lymphocyte responding to non-syngeneic donor antigens)
RN 202475-60-3 CAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 41 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

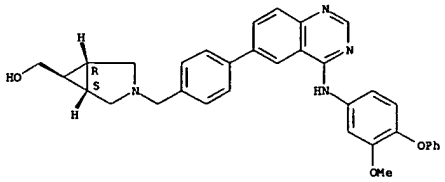


L5 ANSWER 42 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:613804 CAPLUS
DOCUMENT NUMBER: 140:52925
TITLE: The biological and biochemical effects of CP-654577, a selective erbB2 kinase inhibitor, on human breast cancer cells
AUTHOR(S): Barbacci, E. Gabriella; Pustilnik, Leslie R.; Rossi, Ann Marie K.; Emerson, Erling; Miller, Penny E.; Boscoe, Brian P.; Cox, Eric D.; Iwata, Kenneth K.; Jani, Jitesh P.; Provoncha, Kathleen; Kath, John C.; Liu, Zhengyu; Moyer, James D.
CORPORATE SOURCE: Pfizer Global Research and Development, Groton, CT, 06340, USA
SOURCE: Cancer Research (2003), 63(15), 4450-4459
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Aberrant expression or activity of epidermal growth factor receptor (EGFr) or the closely related p185erbB2 can promote cell proliferation and survival and thereby contribute to tumorigenesis. Specific antibodies and low mol.-weight tyrosine kinase inhibitors of both proteins are in clin. trials for cancer treatment. CP-654577 is a potent inhibitor selective for p185erbB2, relative to EGFr tyrosine kinase, and selectively reduces erbB2 autophosphorylation in intact cells. Treatment of SKBr3 human breast cancer cells with CP-654577 reduces the levels of the activated form of mitogen-activated protein kinase, increases the levels of cyclin-dependent kinase inhibitor p27kipl and reduces expression of cyclins D and E. These biochem. changes result in a reduced level of phosphorylated retinoblastoma protein and an inhibition of cell-cycle progression at G1. Apoptosis is triggered in both SKBr3 and another high erbB2-expressing cell line, BT474, by exposure to 1 μM CP-654577, but this effect is not observed in MCF7 cells that express low erbB2. Levels of activated Akt, an important pos. regulator of cell survival, are reduced within 2 h of exposure to 250 nM CP-654577, and this may contribute to the increased apoptosis. These biochem. effects are distinct from those produced by Tarceva, a selective EGFr inhibitor. The antitumor activity of CP-654577 was investigated in athymic mice bearing s.c. tumors from Fischer rat embryo fibroblasts transfected with erbB2. CP-654577 produced a dose-dependent reduction of p185erbB2 autophosphorylation and inhibited the growth of these tumors. CP-654577 warrants further evaluation in tumors with high expression of p185erbB2 and may differ from selective EGFr inhibitors or nonselective dual EGFr/erbB2 inhibitors in efficacy and therapeutic index.

IT **639087-64-2**, CP 654577
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(biol. and biochem. effects of CP-654577, a selective erbB2 kinase inhibitor, on human breast cancer cells)
RN 639087-64-2 CAPLUS
CN 3-Azabicyclo[3.1.0]hexane-6-methanol, 3-[[4-[4-[(3-methoxy-4-phenoxyphenyl)amino]-6-quinazolinyl]phenyl]methyl]-, (1α,5α,6α)- (9CI) (CA INDEX NAME)

Relative stereochemistry.




L5 ANSWER 42 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

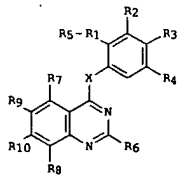
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 43 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:610073 CAPLUS
DOCUMENT NUMBER: 139:144001
TITLE: Preparation of quinazoline derivatives as JAK-3 kinase inhibitors and their therapeutic uses
INVENTOR(S): Fatih, M. Uckun
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 103 pp., Cont.-in-part of U.S. Pat. Appl. 2001 44,442.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2003149045 | A1 | 20030807 | US 2002-211045 | 20020802 |
| US 6313129 | B1 | 20011106 | US 1999-378093 | 19990820 |
| US 2001044442 | A1 | 20011122 | US 2001-812098 | 20010319 |
| US 6495556 | B2 | 20021217 | | |
| US 2002042513 | A1 | 20020411 | US 2001-858824 | 20010516 |
| US 6469013 | B2 | 20021022 | | |

PRIORITY APPLN. INFO.:
US 1999-378093 A1 19990820
US 2001-812098 A2 20010319
US 2001-309557P P 20010802
US 2001-309558P P 20010802
US 1998-97359P P 19980821
US 1998-97365P P 19980821
US 2000-688756 A3 20001016

OTHER SOURCE(S): MARPAT 139:144001
GI




I

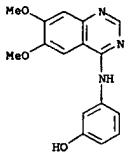
AB The invention provides novel JAK-3 inhibitors that are useful for treating leukemia and lymphoma. The compds. I [X is NH, R11N, S, O, CH2, or R11CH; R11is H, (C1-C4)alkyl, or (C1-C4)alkanoyl; R1-R8 are each independently H, OH, mercapto, NH2, NO, (C1-C4)alkyl, (C1-C4)alkoxy, (C1-C4)alkylthio, or halo; wherein two adjacent groups of R1-R5 together with the Ph ring may optionally form a fused ring that can be substituted; and R9 and R10 are each independently H, (C1-C4)alkyl, (C1-C4)alkoxy, halo, or (C1-C4)alkanoyl; or R9 and R10 together are methylenedioxy] are also useful to treat or prevent skin cancer, as well as sunburn and UVB-induced skin inflammation. In addition, the compds. of the present invention prevent the immunosuppressive effects of UVB radiation, and are useful to treat or prevent autoimmune diseases, inflammation, and transplant rejection. The invention also provides pharmaceutical compns. comprising compds. of the invention, as well as therapeutic methods for their use. Specifically claimed in this CIP patent is a pharmaceutical compn. contg. quinazoline derivs. in combination with methotrexate to treat GVHD.

L5 ANSWER 43 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

IT **572895-68-2**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); **THU (Therapeutic use)**
(GVHD prevention with compns. containing quinazoline derivs. in combination with an immunosuppressant; preparation of quinazoline derivs. as JAK-3 kinase inhibitors and their therapeutic uses)
RN 572895-68-2 CAPLUS
CN L-Glutamic acid, N-[4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl]-, mixt. with 3-[(6,7-dimethoxy-4-quinazolinyl)amino]phenol (9CI) (CA INDEX NAME)

CM 1

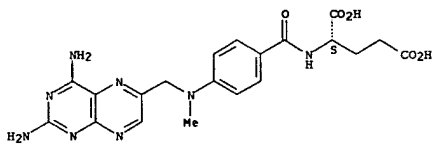
CRN 211555-08-7
CMF C16 H15 N3 O3




CM 2

CRN 59-05-2
CMF C20 H22 N8 O5

Absolute stereochemistry.

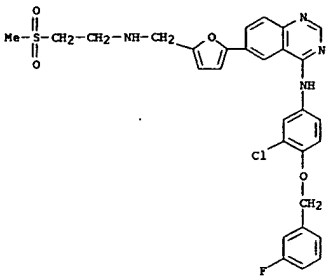


L5 ANSWER 44 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:607455 CAPLUS
DOCUMENT NUMBER: 139:159940
TITLE: Use of tyrosine kinase inhibitors for treatment of pulmonary inflammatory conditions
INVENTOR(S): Jung, Birgit; Puschner, Hubert
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: Ger. Offen., 24 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10204462 | A1 | 20030807 | DE 2002-10204462 | 20020205 |
| WO 2003066060 | A2 | 20030814 | WO 2003-EP814 | 20030128 |
| WO 2003066060 | A3 | 20040115 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1474149 | A2 | 20041110 | EP 2003-704477 | 20030128 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| US 2003149062 | A1 | 20030807 | US 2003-353616 | 20030129 |
| PRIORITY APPLN. INFO.: | | | DE 2002-10204462 A | 20020205 |
| | | | WO 2003-EP814 W | 20030128 |

OTHER SOURCE(S): MARPAT 139:159940
AB The invention discloses the use of quinazoline derivs. (Markush included), or the compds. (1) 4-[(3-chloro-4-fluorphenyl)amino]-6-[(4-dimethylaminocyclohexyl)amino]pyrimido[5,4-d]pyrimidine; (2) 4-[(R)-(1-phenylethyl)amino]-6-(4-hydroxyphenyl)-7H-pyrrolo[2,3-d]pyrimidine; (3) 4-[(3-Chloro-4-(3-fluoro-4-benzyloxy)phenyl)amino]-6-[5-(((2-methansulfonylethyl)amino)methyl)-furan-2-yl]quinazoline; or the antibody cetuximab C225, trastuzumab, ABX-EGF, Mab ICR-62 and EGFR antisense, their tautomers, their stereoisomers and their salts, in particular their physiol. compatible salts with inorg. or organic acids or bases, for the production of a medication for prevention or treatment of diseases of the respiratory system or the lung. Preparation of quinazoline compds. is included.
IT **231277-92-2**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(tyrosine kinase inhibitors for treatment of pulmonary inflammatory conditions)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX

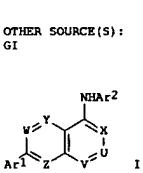
L5 ANSWER 44 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
NAME)



L5 ANSWER 45 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:591156 CAPLUS
DOCUMENT NUMBER: 139:149640
TITLE: Preparation of substituted quinazolin-4-ylamine analogs as VR1 capsaicin receptor antagonists for relieving pain
INVENTOR(S): Bakthavatchalam, Rajagopal; Blum, Charles A.; Brielmann, Harry L.; Caldwell, Timothy M.; De Lombaert, Stephane
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 294 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

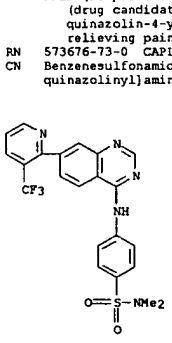
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003062209 | A2 | 20030731 | WO 2003-US1563 | 20030117 |
| WO 2003062209 | A3 | 20030904 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| BR 2003006982 | A | 20041026 | BR 2003-6982 | 20030117 |
| EP 1471910 | A2 | 20041103 | EP 2003-703887 | 20030117 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| US 2004106616 | A1 | 20040603 | US 2003-347210 | 20030121 |
| PRIORITY APPLN. INFO.: | | | US 2002-349920P P | 20020117 |
| | | | US 2002-350527P P | 20020122 |
| | | | WO 2003-US1563 W | 20030117 |

OTHER SOURCE(S): MARPAT 139:149640
GI



AB Substituted quinazolin-4-ylamine analogs (shown as I; variables defined below; e.g. (4-trifluoromethylphenyl)[7-(2-trifluoromethylphenyl)quinazolin-4-yl]amine) are provided. Such compds. are ligands that may be used to modulate VR1 capsaicin receptor activity in vivo or in vitro (no data), and are particularly useful in the treatment of conditions associated with pathol. receptor activation in humans, domesticated companion animals and livestock animals. Pharmaceutical compns. and methods for using them to treat such disorders are provided, as are methods for using such ligands for receptor localization studies. For I; V, X, W, Y and Z are each

L5 ANSWER 45 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
independently N or CR1, with the proviso that at least one of V and X is N; U is N or CR2, with the proviso that if V and X are N, then U is CR2; R1 = H, halogen, hydroxy, amino, C1-C8 alkyl, haloC1-C8alkyl, C1-C8alkoxy, haloC1-C8alkoxy and mono- and di(C1-C8alkyl)amino. R2 = (i) H, halogen, cyano, or -COOH; (ii) C1-C8alkanoyl, C2-C8alkanone, or C1-C8carbamate, each of which is (un)substituted with 1-9 substituents = Rb, or (iii) -Rc-M-A-Ry, wherein: Rc is C0-C3alkyl; M is a bond, N(Rz), O, S, SO2, (C:O)pN(Rz), N(Rz)(C:O)p, SO2N(Rz), or N(Rz)SO2, wherein p is 0 or 1; A is a bond or C1-C8alkyl, (un)substituted with 1-3 Rb. Ry and Rz, if present, are: (a) independently H, C1-C8alkyl, C2-C8alkenyl, C2-C8alkynyl, C6-C10arylC1-C8alkyl, C2-C8alkyl ether, C1-C8alkoxy, a 4- to 10-membered carbocycle or heterocycle, or joined to R1 to form a 4- to 10-membered carbocycle or heterocycle, wherein each Ry and Rz = (un)substituted with 1-9 Rb; or (b) joined to form a 4- to 10-membered carbocycle or heterocycle that is (un)substituted with 1-9 Rb; Ar2 is a 5- to 7-membered arom. heterocycle, (un)substituted with 1-3 LRa. Ar1 is a 5- to 10-membered arom. carbocycle or heterocycle, (un)substituted with 1-3 LRa; L = bond, -O-, -C(O)-, -OC(O)-, -C(O)O-, -O-C(O)O-, -S(O)m-, -NRx-, -C(O)NRx-, -NHRxC(O)-, -NRxS(O)m-, -S(O)mNRx- and -N[S(O)mRx]S(O)m-; wherein m = 0, 1 and 2; and Rx = H and C1-C8alkyl; Ra = (i) H, halogen, cyano and nitro; and (ii) C1-C8alkyl, C2-C8alkenyl, C2-C8alkynyl, C2-C8alkyl ether, 3- to 10-membered heterocycles, mono- and di(C1-C8alkyl)amino and (3- to 10-membered heterocycle)C1-C6 alkyl, each of which is (un)substituted with 1-9 Rb. Rb = hydroxy, halogen, amino, aminocarbonyl, amido, cyano, nitro, C1-C8alkyl, C1-C8alkoxy, C1-C8alkylthio, C1-C8alkyl ether, hydroxyC1-C8alkyl, haloC1-C8alkyl, Ph, phenyl(C1-C8alkyl), mono and di(C1-C6 alkyl)amino, (SO2)C1-C8alkyl, 5- to 7-membered heterocycle and (5- to 7-membered heterocycle)(C1-C8alkyl). Although the methods of prepn. are not claimed, many example prepns. and characterization data for >500 examples of I are included.
IT **573676-73-0P**, N,N-Dimethyl-4-[[7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl]amino]benzenesulfonamide
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate and receptor detector; preparation of substituted quinazolin-4-ylamine analogs as VR1 capsaicin receptor antagonists for relieving pain and for detecting receptors)
RN 573676-73-0 CAPLUS
CN Benzenesulfonamide, N,N-dimethyl-4-[[7-[3-(trifluoromethyl)-2-pyridinyl]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

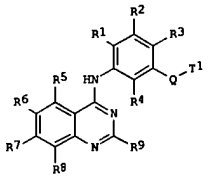


L5 ANSWER 45 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L5 ANSWER 46 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:590835 CAPLUS
DOCUMENT NUMBER: 139:149651
TITLE: Preparation of 4-phenylaminoquinazoline derivatives as fructose 1,6-bisphosphatase inhibitors
INVENTOR(S): Bauer, Paul H.; Wright, Stephen W.; Schnur, Rodney C.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 23 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2003144308 | A1 | 20030731 | US 2002-251073 | 20020920 |
| PRIORITY APPLN. INFO.: | | | US 2001-324751P P | 20010924 |
| OTHER SOURCE(S): | MARPAT 139:149651 | | | |

GI



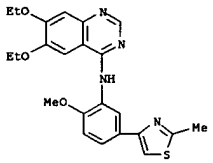
I

AB The present invention relates to certain quinazoline compds. (I), prodrugs thereof, or pharmaceutically acceptable salts of said compds. or said prodrugs, [wherein Q = pyrrolyl, pyrazolyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, triazolyl, furyl, quinolyl, imidazolyl, pyridyl pyrimidyl; T1 = H, Me, Et, OR10, SR10, cyano, cyclopropyl, cyclobutyl, NH2, NHR10, N(R10)2, NHNH2, CHR10OH, CH2R10, COCH3, CON(R10)2; R1, R2, R3, R4 = H, halo, trifluoromethyl, C1-4 alkyl, C1-4 alkoxy; R5, R8 = H, F, Cl, HO, Me; R6, R7 = C1-4 alkyl, C1-4 alkoxy; R9 = H, cyclopropyl, cyclobutyl, C1-4 alkyl, (CH2)m-Y; R10 = H, Me, Et; m = 1, 2, 3, or 4; Y = F, Cl, Br, HO, N(R11)2, N-methylpiperazin-1-yl, thiazolidin-3-yl, thiomorpholin-4-yl, piperidin-1-yl, pyrrolidin-1-yl, morpholin-4-yl, imidazol-1-yl, C1-4 alkoxy, SR11, SOR11, SO2R11, CO2H, CO2(C1-C4)alkyl or CON(R11)2; R11 = H, C1-4 alkyl] which are fructose 1,6-bisphosphatase inhibitors (no data) and have utility in the treatment of **diabetes** mellitus, hypercholesterolemia, hyperlipidemia, diabetic complications, and **cancer**. The invention also relates to pharmaceutical compns. and kits comprising such quinazoline compds. I and to methods of using such compds. in the treatment of **diabetes** mellitus, hypercholesterolemia, hyperlipidemia, diabetic complications, and

L5 ANSWER 46 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
**cancer**. Thus, a soln. of 0.157 g (0.62 mmol) of 4-chloro-6,7-diethoxyquinazoline in 2.5 mL of ethanol was heated at reflux, treated with 0.136 g (0.62 mmol) of 4-(3-aminophenyl)thiazole-2-carboxylic acid amide dissolved in 4 mL of ethanol added in a single portion, and heated at reflux for 30 min, after which the reaction mixt. was allowed to cool and the pptd. product was filtered, washed with ethanol, and dried to afford 0.152 g (56 %) of 4-[3-(6,7-diethoxyquinazolin-4-ylamino)phenyl]thiazole-2-carboxylic acid amide hydrochloride.

IT **460750-82-7P**, (6,7-Diethoxyquinazolin-4-yl)[2-methoxy-5-(2-methylthiazol-4-yl)phenyl]amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylaminoquinazoline derivs. as fructose bisphosphatase inhibitors for treatment of **diabetes** mellitus, hypercholesterolemia, hyperlipidemia, diabetic complications and **cancer**)

RN 460750-82-7 CAPLUS
CN 4-Quinazolinamine, 6,7-diethoxy-N-[2-methoxy-5-(2-methyl-4-thiazolyl)phenyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 47 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:472506 CAPLUS
DOCUMENT NUMBER: 139:41834
TITLE: Preparation of (E)-2-methoxy-N-(3-{4-[3-methyl-4-(6-methylpyridin-3-yloxy)phenylamino]quinazolin-6-yl}allyl)acetamide salts
INVENTOR(S): Richter, Daniel Tyler; Kath, John Charles
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003050108 | A1 | 20030619 | WO 2002-IB4708 | 20021111 |
| WO 2003050108 | C1 | 20031218 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1456199 | A1 | 20040915 | EP 2002-804543 | 20021111 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002014876 | A | 20041228 | BR 2002-14876 | 20021111 |
| US 2003158217 | A1 | 20030821 | US 2002-315862 | 20021210 |
| US 6844349 | B2 | 20050118 | | |
| PRIORITY APPLN. INFO.: | | | US 2001-340885P P | 20011212 |
| | | | WO 2002-IB4708 W | 20021111 |

AB The invention relates to succinate and malonate salts of (E)-2-methoxy-N-(3-(4-[3-methyl-4-(6-methyl-pyridin-3-yloxy)phenylamino]quinazolin-6-yl}allyl)acetamide (I). More particularly, the present invention relates to pharmaceutical compns. containing sesqui-succinate and dimalonate salts of I. The invention further relates to methods of treating hyperproliferative diseases, such as cancers, in mammals, especially humans by administering the above salts. A salt was prepared by the reaction of the quinazolinylallylacetamide derivative with malonic acid.

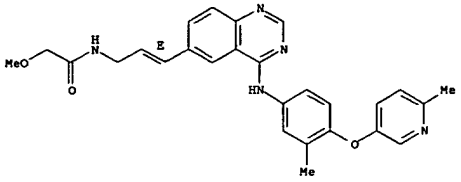
IT **543681-31-8P**
RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of methoxy(methyl(methylpyridinyloxy)phenylamino)quinazolinylallylacetamide salts)

RN 543681-31-8 CAPLUS
CN Butanedioic acid, compd. with 2-methoxy-N-[(2E)-3-[4-[[3-methyl-4-[(6-methyl-3-pyridinyl)oxy]phenyl]amino]-6-quinazolinyl]-2-propenyl]acetamide (3:2) (9CI) (CA INDEX NAME)

CM 1

CRN 383432-38-0
CMF C27 H27 N5 O3

L5 ANSWER 47 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
Double bond geometry as shown.



CM 2

CRN 110-15-6
CMF C4 H6 O4

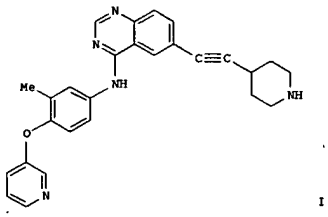
$HO_2C-CH_2-CH_2-CO_2H$

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 48 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:472389 CAPLUS
DOCUMENT NUMBER: 139:36543
TITLE: Preparation of quinazoline derivatives for the treatment of abnormal cell growth
INVENTOR(S): Kath, John Charles; Moyer, James Dale; Connell, Richard Damian
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003049740 | A1 | 20030619 | WO 2002-IB4636 | 20021104 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1465632 | A1 | 20041013 | EP 2002-777736 | 20021104 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| US 2003171386 | A1 | 20030911 | US 2002-315863 | 20021210 |
| PRIORITY APPLN. INFO.: | | | US 2001-341091P | P 20011212 |
| | | | WO 2002-IB4636 | W 20021104 |

OTHER SOURCE(S): MARPAT 139:36543
GI



I

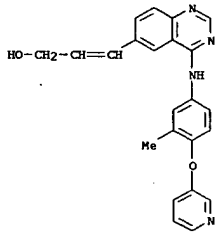
L5 ANSWER 48 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

AB This invention relates to quinazoline derivs. that are useful in the treatment of abnormal cell growth, such as **cancer**, in mammals. For instance, 4-ethynylpiperidine-1-carboxylic acid tert-Bu ester is coupled to 4-chloro-6-iodoquinazoline (THF, i-Pr2NH, (Ph3P)2PdCl2, CuI) and the product reacted with 3-Methyl-4-[pyridin-3-yloxy]phenylamine (dichloroethane, t-BuOH, 90°) and finally treated with HCl gas to give I. The invention further relates to small mols. that are selective for erbB2 receptor over the erbB1 receptor, wherein said erbB2 inhibitor has a range of selectivities for erbB2 over erbB1 between 50-1500.

IT **383430-50-0P**, 3-[4-[[3-Methyl-4-[pyridin-3-yloxy]phenyl]amino]quinazolin-6-yl]prop-2-en-1-ol
RL: PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(quinazoline derivs. for treatment of abnormal cell growth)

RN 383430-50-0 CAPLUS

CN 2-Propen-1-ol, 3-[4-[[3-methyl-4-(3-pyridinyloxy)phenyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

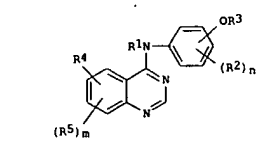


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 49 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:434552 CAPLUS
DOCUMENT NUMBER: 139:22223
TITLE: Processes for the preparation of substituted arylaminoquinazolines for the treatment of abnormal cell growth
INVENTOR(S): Ripin, David Harold Brown
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003045939 | A1 | 20030605 | WO 2002-IB4097 | 20021003 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1448551 | A1 | 20040825 | EP 2002-772689 | 20021003 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002014606 | A | 20040914 | BR 2002-14606 | 20021003 |
| US 2003144506 | A1 | 20030731 | US 2002-307603 | 20021202 |
| PRIORITY APPLN. INFO.: | | | US 2001-334647P | P 20011130 |
| | | | WO 2002-IB4097 | W 20021003 |

OTHER SOURCE(S): MARPAT 139:22223
GI



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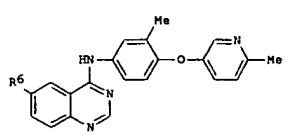


II

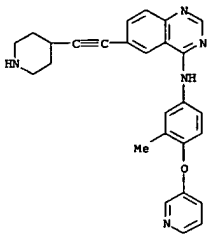
L5 ANSWER 49 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

AB Arylaminoquinazolines I [R1 = H, alkyl; R2 = halo, CN, NO2, F3CO, F3C, N3, (un)substituted OH, NH2, alkyl, alkenyl, alkynyl, acyl; R3 = heterocyclyl, heterocyclylalkyl; R4 = (un)substituted alkynyl, alkenyl; R5 = halo, (un)substituted OH NH2, alkyl, CONH2, SO2NH2; m = 0-3; n = 0-4] were prepared for use in treating abnormal cell growth in mammals (no data). Thus, 4-chloro-6-iodoquinazoline was treated with 3-(4-amino-2-methylphenoxy)-6-methylpyridine to give the aminoquinazoline II [R6 = I] which was treated with MeOCH2CONHCH2C.tplbond.CH under Suzuki coupling conditions to give II [R6 = MeOCH2CONHCH2CH:CH].

IT **383430-46-4P**
RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(processes for the preparation of substituted arylaminoquinazolines for the treatment of abnormal cell growth)

RN 383430-46-4 CAPLUS

CN 4-Quinazolinamine, N-[3-methyl-4-(3-pyridinyloxy)phenyl]-6-(4-piperidinylethynyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 50 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:376831 CAPLUS
DOCUMENT NUMBER: 138:385442
TITLE: Preparation of (anilino)quinazolines as antitumor agents
INVENTOR(S): Hennequin, Laurent Francois Andre; Kettle, Jason Grant; Pass, Martin; Bradbury, Robert Hugh
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 275 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003040109 | A2 | 20030515 | WO 2002-GB4932 | 20021031 |
| WO 2003040109 | A3 | 20030626 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1444211 | A2 | 20040811 | EP 2002-774961 | 20021031 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002013843 | A | 20040831 | BR 2002-13843 | 20021031 |
| PRIORITY APPLN. INFO.: | | | GB 2001-26433 A | 20011103 |
| | | | WO 2002-GB4932 W | 20021031 |

OTHER SOURCE(S): MARPAT 138:385442

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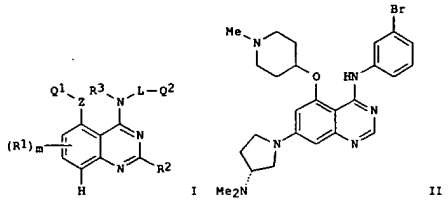


AB Title compds. I [wherein m = 0-2; n = 1-2; L = a bond or {C(R22)2}n; R1 =

L5 ANSWER 50 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

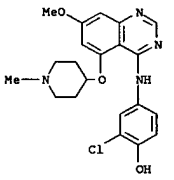
halo, CF3, CN, NC, NO2, OH, SH, NH2, CHO, CO2H, CONH2, or (un)substituted alkyl(oxy), alkenyl(oxy), alkynyl(oxy), alkylthio, alkylsulfinyl, alkylsulfonyl, (di)alkylamino, alkoxycarbonyl, (di)alkylcarbamoyl, alkanoyl(oxy), (alkyl)alkanoylamino, (alkyl)alkenoylamino, (alkyl)alkynoylamino, (di)alkylsulfamoyl, (alkyl)alkanesulfonylamino, or Q3X1; or (R1)m = alkylenedioxy; with the proviso that adjacent alkylene C atoms within a R1 substituent are optionally interrupted by O, S, SO, SO2, NR5, CO, CHOR5, CONR5, NR5CO, SO2NR5, NR5SO2, CH=CH, or C.tplbond.C; R2 = H; R3, R4, R5, R11, R12, and R22 = independently H or alkyl; Q1 and Q3 = independently (un)substituted (hetero)aryl(alkyl), cycloalkyl(alkyl), cycloalkenyl(alkyl), or heterocyclyl(alkyl); with the proviso that adjacent alkylene C atoms within the Q12 group are optionally interrupted by O, S, SO, SO2, NR12, CO, CHOR12, CONR12, NR12CO, SO2NR12, NR12SO2, CH=CH, or C.tplbond.C; Q2 = (un)substituted Ph, bicyclic (hetero)aryl, or bicyclic heterocyclyl; X1 = a bond, O, S, SO, SO2, NR4, CO, CHOR4, CONR4, NR4CO, SO2NR4, NR4SO2, OC(R4)2, SC(R4)2, or NR4C(R4)2; Z = a bond, O, S, SO, SO2, NR11, CO, CHOR11, CONR11, NR11CO, SO2NR11, NR11SO2, OC(R11)2, SC(R11)2, or NR11C(R11)2; and pharmaceutically acceptable salts thereof} were prepd. for use in the prevention or treatment of tumors which are sensitive to inhibition of erbB receptor tyrosine kinases. For example, coupling of 3-(R)-(+)-dimethylaminopyrrolidine with 3,4-dihydro-5-hydroxy-7-fluoroquinazolin-4-one=CF3CO2H in NMP gave the pyrrolidinylquinazolinone (41%). Addn. of chloromethyl pivalate in the presence of NaH in DMF afforded the 3-substituted deriv. (62%), which was condensed with 4-hydroxy-N-methylpiperidine using PPh3 and di-tert-Bu azodicarboxylate in DCM to give the piperidinyloxyquinazolinone (77%). Deprotection (66%) using NH3 in MeOH, followed by chlorination with POCl3 and di-diisopropylethylamine in dichloroethane provided 4-chloro-7-(3-(R)-dimethylaminopyrrolidin-1-yl)-5-(1-methylpiperidin-4-yloxy)quinazoline (81%). Coupling of the chloroquinazoline with 3-bromoaniline in the presence of HCl and IPA in dioxane yielded II•HCl (43%). The biol. activity of the example compds. was assessed in five assays. Thus, I inhibited the phosphorylation of a tyrosine-contg. polypeptide substrate by epidermal growth factor receptor (EGFR) kinase, erbB2 kinase, and erbB4 kinase with IC50 values in the range of 0.001 μM - 10 μM. I also inhibited the proliferation of both human naso-pharyngeal carcinoma KB cells and non-neoplastic epithelial H16N-2 cells with IC50 values in the range 0.001 μM - 20 μM. In addn., I inhibited the growth of colorectal adenocarcinoma LoVo and human mammary carcinoma BT-474 tumor cell xenografts in vivo with activities in the range of 1 mg/kg/day to 200 mg/kg/day with no physiol. unacceptable toxicity at the ED.

IT **525590-37-8P**, 4-(3-Chloro-4-hydroxyanilino)-7-methoxy-5-(1-methylpiperidin-4-yloxy)quinazoline
RL: PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(antitumor agent; preparation of (anilino)quinazolines as erbB receptor tyrosine kinase inhibitors for treatment of cancer)

RN 525590-37-8 CAPLUS

CN Phenol, 2-chloro-4-[[7-methoxy-5-[(1-methyl-4-piperidinyl)oxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 50 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



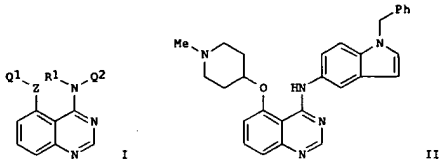
L5 ANSWER 51 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:376830 CAPLUS
DOCUMENT NUMBER: 138:385441
TITLE: Preparation of quinazolines as antitumor agents
INVENTOR(S): Hennequin, Laurent Francois Andre; Kettle, Jason Grant; Pass, Martin; Bradbury, Robert Hugh
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 218 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003040108 | A1 | 20030515 | WO 2002-GB4931 | 20021031 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1444210 | A1 | 20040811 | EP 2002-774960 | 20021031 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002013842 | A | 20040831 | BR 2002-13842 | 20021031 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| GB 2001-26433 | A | 20011103 |
| GB 2001-29059 | A | 20011205 |
| WO 2002-GB4931 | W | 20021031 |

OTHER SOURCE(S): MARPAT 138:385441
GI



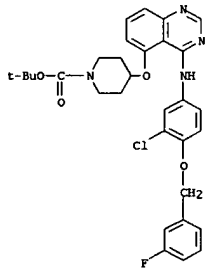
I II

AB Anilino-, indolylamino-, and benzopyrazolylamino-substituted quinazolines I [wherein R1, R2, R3, and R6 = independently H or alkyl; Z = a bond, O, S, or NR2; Q1 = (un)substituted cycloalkyl(alkyl), cycloalkyl(alkenyl), cycloalkyl(alkynyl), or heterocyclyl(alkyl); with the proviso that alkylene chains within Q1Z are optionally interrupted by O, S, SO, SO2, NR3, CO, CHOR3, CONR3, NR3CO, SO2NR3, NR3SO2, CH=CH, or C.tplbond.C; Q2 = (un)substituted C6H4-4-X2Q2, 1-(X3Q4)indol-5-yl, 1-(X3Q4)-indol-6-yl, 1-(X3Q4)-1H-benzopyrazol-5-yl, or 1-(X3Q4)-1H-benzopyrazol-6-yl; X2 = a bond, O, S, SO, SO2, NR6, CHOR6, CONR6, NR6CO, SO2NR6, NR6SO2, OC(R6)2, C(R6)2O, SC(R6)2, C(R6)2S, CO, C(R6)2NR6, or NR6C (R6)2; or X2Q3 = heterocyclylcarbonyl; X3 = a bond, SO2, CO, SO2NR7, or C(R7)2; Q3 and Q4 = independently (un)substituted (heteroaryl); and pharmaceutically acceptable salts thereof] were prepd. for use in the prevention or treatment of tumors which are sensitive to inhibition of erbB receptor tyrosine kinases. For example, coupling of 4-hydroxy-1-methylpiperidine with 5-fluoro-3,4-dihydroquinazolin-4-one using NaH in DMA gave the ether (91%). Reaction with POCl3 and di-isopropylethylamine in DCM provided 4-chloro-5-(1-methylpiperidin-4-yloxy)quinazoline (62%), which was coupled with 5-amino-1-benzylindole in the presence of IPA contg. HCl in ether to afford II•HCl (46%). The biol. activity of the example compds. was assessed in five assays. Thus, I inhibited the phosphorylation of a tyrosine-contg. polypeptide substrate by epidermal growth factor receptor (EGFR) kinase, erbB2 kinase, and erbB4 kinase with IC50 values in the range of 0.001 μM - 10 μM. I also inhibited the **proliferation** of both human naso-pharyngeal carcinoma KB cells and non-**neoplastic** epithelial H16N-2 cells with IC50 values in the range 0.001 μM - 20 μM. In addn., I inhibited the growth of colorectal adenocarcinoma LoVo and human mammary carcinoma BT-474 **tumor** cell xenografts in vivo with activities in the range of 1 mg/kg/day to 200 mg/kg/day with no physiol. unacceptable toxicity at the ED.

IT **524953-85-3P**, 5-[1-(tert-Butoxycarbonyl)piperidin-4-yloxy]-4-[3-chloro-4-(3-fluorobenzyloxy)anilino]quinazoline
RL: PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(antitumor agent; preparation of quinazolines as erbB receptor tyrosine kinase inhibitors for treatment of **cancer**)

RN 524953-85-3 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[[4-[[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]amino]-5-quinazolinyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L5 ANSWER 51 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



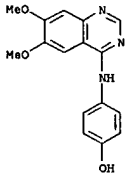
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 52 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:293677 CAPLUS
DOCUMENT NUMBER: 139:301736
TITLE: Targeting JAK3 with JANEX-1 for prevention of autoimmune type 1 **diabetes** in NOD mice
AUTHOR(S): Cetkovic-Cvrlje, Marina; Dragt, Angela L.; Vassilev, Alexei; Liu, Xing-Ping; Uckun, Fatih M.
CORPORATE SOURCE: Department of Immunology, Parker Hughes Institute, St. Paul, MN, 55113, USA
SOURCE: Clinical Immunology (San Diego, CA, United States) (2003), 106(3), 213-225
CODEN: CLIIFY; ISSN: 1521-6616
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Here we show that Janus kinase (JAK) 3 is an important mol. target for treatment of autoimmune insulin-dependent (type 1) **diabetes** mellitus. The rationally designed JAK3 inhibitor JANEX-1 exhibited potent immunomodulatory activity and delayed the onset of **diabetes** in the NOD mouse model of autoimmune type 1 **diabetes**. Whereas 60% of vehicle-treated control NOD mice became diabetic by 25 wk, the incidence of **diabetes** at 25 wk was only 9% for NOD females treated with daily injections of JANEX-1 (100 mg/kg/day) from Week 10 through Week 25 (P = 0.007). Furthermore, JANEX-1 prevented the development of insulitis and **diabetes** in NOD-scid/scid females after adoptive transfer of splenocytes from diabetic NOD females. Chemical inhibitors such as JANEX-1 may provide the basis for effective treatment modalities against human type 1 **diabetes**. To our knowledge, this is the first report of the immunosuppressive activity of a JAK3 inhibitor in the context of an autoimmune disease.

IT **202475-60-3P**, JANEX 1
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(JANEX-1 prevention of autoimmune type 1 **diabetes** mediated by JAK3)

RN 202475-60-3 CAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 53 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

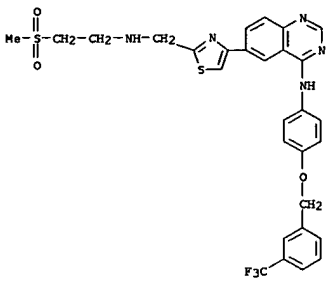
ACCESSION NUMBER: 2003:189366 CAPLUS
DOCUMENT NUMBER: 139:62609
TITLE: Discovery and Biological Evaluation of Potent Dual ErbB-2/EGFR Tyrosine Kinase Inhibitors: 6-Thiazolylquinazolines
AUTHOR(S): Gaul, Micheal D.; Guo, Yu; Affleck, Karen; Cockerill, G. Stuart; Gilmer, Tona M.; Griffin, Robert J.; Guntrip, Stephen; Keith, Barry R.; Knight, Wilson B.; Mullin, Robert J.; Murray, Doris M.; Rusnak, David W.; Smith, Kathryn; Tadepalli, Sarva; Wood, Edgar R.; Lackey, Karen
CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(4), 637-640
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:62609

AB We have identified a novel class of 6-thiazolylquinazolines as potent and selective inhibitors of both ErbB-2 and EGFR tyrosine kinase activity, with IC50 values in the nanomolar range. These compds. inhibited the growth of both EGFR (HN5) and ErbB-2 (BT474) over-expressing human tumor cell lines in vitro. Using xenograft models of the same cell lines, we found that the compds. given orally inhibited in vivo tumor growth significantly compared with control animals.

IT **231277-87-5P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6-thiazolylquinazolines as dual ErbB-2/EGFR tyrosine kinase inhibitors for use in cancer treatment)

RN 231277-87-5 CAPLUS
CN 4-Quinazolinamine, 6-[2-[[[2-(methylsulfonyl)ethyl]amino]methyl]-4-thiazolyl]-N-[4-[[3-(trifluoromethyl)phenyl]methoxy]phenyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 53 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

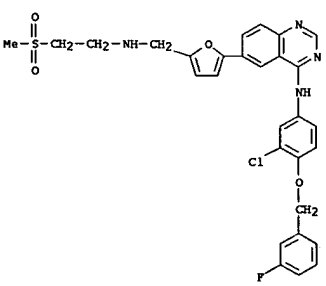
L5 ANSWER 54 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:8967 CAPLUS
DOCUMENT NUMBER: 139:62338
TITLE: Small molecule tyrosine kinase inhibitors: clinical development of anticancer agents
AUTHOR(S): Laird, A. Douglas; Cherrington, Julie M.
CORPORATE SOURCE: SUGEN, Inc., South San Francisco, CA, 94080, USA
SOURCE: Expert Opinion on Investigational Drugs (2003), 12(1), 51-64
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Numerous small mol. synthetic tyrosine kinase inhibitors are in clin. development for the treatment of human cancers. These fall into three broad categories: inhibitors of the epidermal growth factor receptor tyrosine kinase family (e.g., Iressa and Tarceva), inhibitors of the split kinase domain receptor tyrosine kinase subgroup (e.g., PTK787/ZK 222584 and SU11248) and inhibitors of tyrosine kinases from multiple subgroups (e.g., Gleevec). In addition, agents targeting other tyrosine kinases implicated in cancer, such as Met, Tie-2 and Src, are in preclin. development. As experience is gained in the clinic, it has become clear that unleashing the full therapeutic potential of tyrosine kinase inhibitors will require patient preselection, better assays to guide dose selection, knowledge of mechanism-based side effects and ways to predict and overcome drug resistance.

IT **231277-92-2**, GW-572016
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small mol. tyrosine kinase inhibitors and clin. development of anticancer agents)

RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 127 THERE ARE 127 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

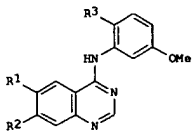
L5 ANSWER 54 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L5 ANSWER 55 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:888722 CAPLUS
DOCUMENT NUMBER: 137:384857
TITLE: Preparation of 4-anilinoquinazolines as antitumor agents
INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002092579 | A1 | 20021121 | WO 2002-GB2128 | 20020508 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2001-401221 A 20010514
OTHER SOURCE(S): MARPAT 137:384857
GI

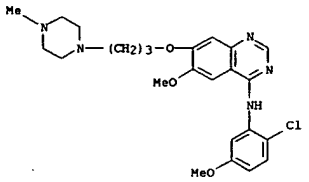


I

AB The title compds. [I; R1 = H, OH, alkoxy and R2 = hydroxyalkoxy, alkoxyalkoxy, aminoalkoxy, etc.; or R2 = H, OH, alkoxy and R1 = hydroxyalkoxy, alkoxyalkoxy, aminoalkoxy, etc.; R3 = Cl, Br, I], useful as an anti-invasive agents in the containment and/or treatment of solid tumor disease, were prepared and formulated. E.g., a multi-step synthesis of I.2HCl [R1 = OMe; R2 = 3-(4-methylpiperazin-1-yl)propoxy; R3 = Cl], starting from 2-amino-4-benzyloxy-5-methoxybenzamide, was given. The biol. activity of compds. I was tested in 4 tests. Thus, the compds. I showed IC50 of 0.001-10 μM in in vitro c-Src tyrosine kinase assay.

IT **476156-74-8P**, 4-(2-Chloro-5-methoxyanilino)-6-methoxy-7-[3-(4-methylpiperazin-1-yl)propoxy]quinazoline dihydrochloride salt
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES

L5 ANSWER 55 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
(Uses)
(prepn. of 4-anilinoquinazolines as antitumor agents)
RN 476156-74-8 CAPLUS
CN 4-Quinazolinamine, N-(2-chloro-5-methoxyphenyl)-6-methoxy-7-[3-(4-methyl-1-piperazinyl)propoxy]-, dihydrochloride (9CI) (CA INDEX NAME)



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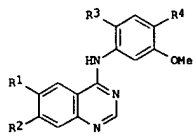
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 56 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:888721 CAPLUS
DOCUMENT NUMBER: 137:384856
TITLE: Preparation of 4-anilinoquinazolines as antitumor agents
INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002092578 | A1 | 20021121 | WO 2002-GB2124 | 20020508 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2001-401222 A 20010514
OTHER SOURCE(S): MARPAT 137:384856
GI

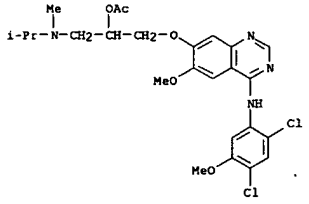


I

AB The title compds. [I; R1 = H, alkoxy and R2 = X1Q1 (wherein X1 = O, S, SO, etc.; Q1 = heteroaryl, heteroarylalkyl, heterocyclyl, etc.), X2R5 (wherein X2 = O, NH, Nalkyl; R5 = hydroxyalkyl, alkoxyalkyl, aminoalkyl, etc.); or R2 = H, alkoxy and R1 = X1Q1, X2R5; R3, R4 = Cl, Br, I], useful as anti-invasive agents in the containment and/or treatment of solid tumor disease, were prepared and formulated. E.g., a multi-step synthesis of I.2HCl [R1 = OMe; R2 = N-methylpiperidin-4-ylmethoxy; R3, R4 = Cl], starting from Et piperidine-4-carboxylate, was given. Biol. activity of compds. I was tested in 4 tests. Thus, the compds. I showed IC50 of 0.001-10 μM in in vitro c-Src tyrosine kinase assay.

IT **476162-63-7P**
RL: PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 4-anilinoquinazolines as antitumor agents)

L5 ANSWER 56 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RN 476162-63-7 CAPLUS
CN 2-Propanol, 1-[[4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]-3-[methyl(1-methylethyl)amino]-, acetate (ester), dihydrochloride (9CI) (CA INDEX NAME)



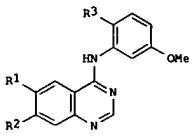
●2 HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 57 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:888720 CAPLUS
DOCUMENT NUMBER: 137:384855
TITLE: Preparation of 4-anilinoquinazolines as antitumor agents
INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

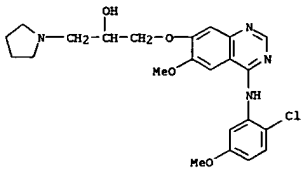
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002092577 | A1 | 20021121 | WO 2002-GB2117 | 20020508 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: EP 2001-401223 A 20010514
OTHER SOURCE(S): MARPAT 137:384855
GI



I

AB The title compds. {I; R1 = H, alkoxy and R2 = X1Q1 (wherein X1 = O, S, SO, etc.; Q1 = heteroaryl, heteroarylalkyl, heterocyclyl, etc.), X2R5 (wherein X2 = O, NH, Nalkyl; R5 = hydroxyalkyl, alkoxyalkyl, aminoalkyl, etc.); or R2 = H, alkoxy and R1 = X1Q1, X2R5; R3 = Cl, Br, I], useful as anti-invasive agents in the containment and/or treatment of solid tumor disease, were prepared and formulated. E.g., a multi-step synthesis of I [R1 = OMe; R2 = N-methylpiperidin-4-ylmethoxy; R3 = Cl], starting from Et piperidine-4-carboxylate, was given. Biol. activity of compds. I was tested in 4 tests. Thus, the compds. I showed IC50 of 0.001-10 μM in in vitro c-Src tyrosine kinase assay.
IT **476160-16-4P**, 4-(2-Chloro-5-methoxyanilino)-7-(2-hydroxy-3-pyrrolidin-1-ylpropoxy)-6-methoxyquinazoline
RL: PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 4-anilinoquinazolines as antitumor agents)
RN 476160-16-4 CAPLUS
CN 1-Pyrrolidineethanol, α-[[[4-[(2-chloro-5-methoxyphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]- (9CI) (CA INDEX NAME)



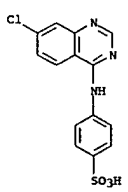
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 58 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:869496 CAPLUS
DOCUMENT NUMBER: 137:363033
TITLE: Peptidomimetic modulators of cell adhesion
INVENTOR(S): Gour, Barbara J.; Blaschuk, Orest W.; Ali, Anmar; Ni, Feng; Chen, Zhigang; Michaud, Stephanie D.; Wang, Shoameng; Hu, Zenjian
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 309 pp., Cont.-in-part of U.S. Ser. No. 491,078.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2002168761 | A1 | 20021114 | US 2001-769145 | 20010124 |
| US 2004058864 | A1 | 20040325 | US 2003-412701 | 20030410 |
| US 2004006011 | A1 | 20040108 | US 2003-425557 | 20030428 |

PRIORITY APPLN. INFO.:
US 2000-491078 A2 20000124
US 1996-21612P P 19960712
US 1997-893534 A1 19970711
US 2000-507102 A1 20000217
US 2001-769145 B1 20010124
US 2001-6982 A2 20011204

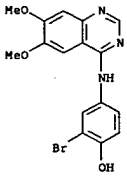
OTHER SOURCE(S): MARPAT 137:363033
AB Peptidomimetics of cyclic peptides, and compns. comprising such peptidomimetics are provided. The peptidomimetics have a three-dimensional structure that is substantially similar to a three-dimensional structure of a cyclic peptide that comprises a cadherin cell adhesion recognition sequence HAV. Methods for using such peptidomimetics for modulating cadherin-mediated cell adhesion in a variety of contexts are also provided.
IT **105037-36-3**, Benzenesulfonic acid, 4-[(7-chloro-4-quinazolinyl)amino]-
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(peptidomimetic modulators of cadherin-mediated cell adhesion for therapeutic use in relation to three-dimensional structure)
RN 105037-36-3 CAPLUS
CN Benzenesulfonic acid, 4-[(7-chloro-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L5 ANSWER 59 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:694236 CAPLUS
DOCUMENT NUMBER: 138:248178
TITLE: Augmentation of mast cell bactericidal activity by the anti-leukemic drug, 4-(3'-bromo-4'-hydroxylphenyl)amino-6,7-dimethoxyquinazoline
AUTHOR(S): Malaviya, Ravi; Navara, Christopher; Uckun, Fatih M.
CORPORATE SOURCE: Department of Allergy and Inflammatory Diseases, Parker Hughes Cancer Center, St. Paul, MN, 55113, USA
SOURCE: Leukemia & Lymphoma (2002), 43(6), 1329-1332
CODEN: LELYEA; ISSN: 1042-8194
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mast cells play a pivotal role in host innate immune defense against gram neg. bacterial infections by killing gram neg. bacteria and recruiting neutrophils to the sites of active infection through the release of TNFα and leukotrienes. Here, we report that the antileukemic compound 4-(3'-bromo-4'-hydroxylphenyl)amino-6,7-dimethoxyquinazoline, designated as MASTPROM, augments the bactericidal activity of mast cells by increasing the binding of bacteria to and their phagocytosis by mast cells. MASTPROM also promoted the bacterial clearance in a mouse model of bacterial peritonitis. MASTPROM may provide the basis for novel supportive care regimens aimed at augmenting the bactericidal activity of mast cells and thereby potentiating the innate immune response against gram neg. organisms.

IT 211555-04-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(augmentation of mast cell bactericidal activity by the antileukemic drug, (bromohydroxylphenyl)aminodimethoxyquinazoline)
RN 211555-04-3 CAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



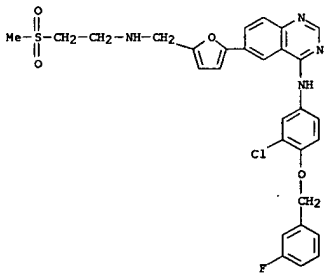

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 60 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:668812 CAPLUS
DOCUMENT NUMBER: 138:280796
TITLE: Anti-tumor activity of GW572016: a dual tyrosine kinase inhibitor blocks EGF activation of EGFR/erbB2 and downstream Erk1/2 and AKT pathways
AUTHOR(S): Xia, Wenle; Mullin, Robert J.; Keith, Barry R.; Liu, Lei-Hua; Ma, Hong; Rusnak, David W.; Owens, Gary; Alligood, Krystal J.; Spector, Neil L.
CORPORATE SOURCE: GlaxoSmithKline, Department of Discovery Medicine, Research Triangle Park, North Carolina, NC, 27709-3398, USA
SOURCE: Oncogene (2002), 21(41), 6255-6263
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dual EGFR/erbB2 inhibition is an attractive therapeutic strategy for epithelial tumors, as ligand-induced erbB2/EGFR heterodimerization triggers potent proliferative and survival signals. Here we show that a small mol., GW572016, potently inhibits both EGFR and erbB2 tyrosine kinases leading to growth arrest and/or apoptosis in EGFR and erbB2-dependent tumor cell lines. GW572016 markedly reduced tyrosine phosphorylation of EGFR and erbB2, and inhibited activation of Erk1/2 and AKT, downstream effectors of proliferation and cell survival, resp. Complete inhibition of activated AKT in erbB2 overexpressing cells correlated with a 23-fold increase in apoptosis compared with vehicle controls. EGF, often elevated in cancer patients, did not reverse the inhibitory effects of GW572016. These observations were reproduced in vivo, where GW572016 treatment inhibited activation of EGFR, erbB2, Erk1/2 and AKT in human tumor xenografts. Erk1/2 and AKT represent potential biomarkers to assess the clin. activity of GW572016. Inhibition of activated AKT in EGFR or erbB2-dependent tumors by GW572016 may lead to tumor regressions when used as a monotherapy, or may enhance the anti-tumor activity of chemotherapeutics, since constitutive activation of AKT has been linked to chemo-resistance.

IT 231277-92-2, GW 572016
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GW572016 antitumor activity: dual tyrosine kinase inhibitor blocks EGF activation of EGFR/erbB2 and downstream Erk1/2 and AKT pathways)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 60 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)




REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 61 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:658094 CAPLUS
DOCUMENT NUMBER: 137:185509
TITLE: Preparation of 4-phenylaminoquinazoline derivatives as inhibitors of tyrosine-specific protein kinase
INVENTOR(S): Kitano, Yasunori; Kawahara, Eiji; Suzuki, Tsuyoshi; Abe, Daisuke; Nakajou, Masahiro; Ueda, Naoko
PATENT ASSIGNEE(S): Mitsubishi Pharma Corporation, Japan
SOURCE: PCT Int. Appl., 154 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002066445 | A1 | 20020829 | WO 2002-JP1575 | 20020221 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2442742 | AA | 20020829 | CA 2002-2442742 | 20020221 |
| EP 1369418 | A1 | 20031210 | EP 2002-700688 | 20020221 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2004116422 | A1 | 20040617 | US 2003-468788 | 20030821 |
| PRIORITY APPLN. INFO.: | | | JP 2001-45827 A | 20010221 |
| | | | JP 2001-353525 A | 20011119 |
| | | | WO 2002-JP1575 W | 20020221 |

OTHER SOURCE(S): MARPAT 137:185509
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

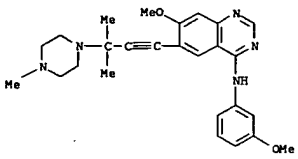
AB Compds. represented by the following general formula (I) or pharmaceutically acceptable salts thereof, hydrates or solvates of the same or mixts. of optically active isomers, racemic compds. or diastereomers of the same [n = an integer of 0-3; R1 = H, halo, HO, cyano, NO2, CF3, C1-5 alkyl, C1-5 alkoxy, S(O)f-C1-5 alkyl (wherein f = an integer of 0-2), (un)substituted NH2; one of R2 and R2 is R27SO2NH, (R28SO2)2N, C1-5 alkoxy, MeCOCH2CONH, MeSCH2CH2OCONH, or NCCH2CONH, etc. (wherein R27, R28 = optionally morpholino-substituted C1-5 alkyl) and the other one represents Y(CR12R13)mCR8R9C.tplbond.C, Y(CR12R13)mCR8R9CH:CH, Q, Q1 (wherein R8, R9 = H, optionally HO- or C1-5 alkoxy substituted C1-5 alkyl, or CR8 R9 together represent CO or C3-8 cycloalkylene optionally interrupted by O, S, NH, or alkyl-N; Y = H,HO, C1-5 alkoxy, C1-5 alkanoyloxy, etc.; R11, R12 = H, C1-5 alkyl; m = an integer of 0-3; p, q = 2,3; Z = O, S, SO, SO2, CO, optionally substituted NH; p1, p2 = an integer of 1-3; n1 = 0,1; W = H,HO, C1-5 alkoxy, C1-5 alkanoyloxy, CO2H, cyano, di-C1-5 alkyamino, morpholino, etc.)] are prepared These compds. have an excellent protein kinase inhibitory activity specific to tyrosine and, therefore, are usable as drugs, in particular, remedies/preventives for

L5 ANSWER 61 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
various cancers, diseases caused by arteriosclerosis or psoriasis. Thus, 1-(1,1-dimethyl-2-propynyl)-4-methylpiperazine was treated with 4,4,5,5-tetramethyl-1,3,2-dioxaborane in the presence of PhCl(PPh3)3 in THF/CH2Cl2 at room temp. and coupled with 4-(3-chloro-4-fluorophenylamino)-6-methoxy-7-quinazolinyl triflate (prepn. given) in the presence of PdCl2(dppf).CH2Cl2 [dppf = 1,1'-bis(diphenylphosphino)ferrocene] in a mixt. of DMF and 2 m aq. Na2CO3 80° for 1 h to give the title compd. (II). II.HCl showed IC50 of 0.82 nM against EGF receptor tyrosine kinase.

IT **451493-48-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylaminoquinazoline derivs. as inhibitors of tyrosine-specific protein kinase for preparation and/or treatment of cancers, diseases caused by arteriosclerosis, or psoriasis)

RN 451493-48-4 CAPLUS

CN 4-Quinazolinamine, 7-methoxy-N-(3-methoxyphenyl)-6-[3-methyl-3-(4-methyl-1-piperazinyl)-1-butynyl]- (9CI) (CA INDEX NAME)




REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 62 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:555376 CAPLUS
DOCUMENT NUMBER: 137:119644
TITLE: 4-Quinazolineamine derivative combination with other antineoplastic agent for **cancer** treatment, and compound preparation.
INVENTOR(S): Lackey, Karen Elizabeth; Spector, Neil; Wood, Edgar Raymond, III; Xia, Wenle
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002056912 | A2 | 20020725 | WO 2002-US1130 | 20020114 |
| WO 2002056912 | A3 | 20030522 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1353693 | A2 | 20031022 | EP 2002-703127 | 20020114 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004523522 | T2 | 20040805 | JP 2002-557419 | 20020114 |
| EP 1488809 | A1 | 20041222 | EP 2004-77577 | 20020114 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR | | | | |
| US 2004053946 | A1 | 20040318 | US 2003-466290 | 20030715 |
| PRIORITY APPLN. INFO.: | | | US 2001-262402P | P 20010116 |
| | | | EP 2002-703127 | A3 20020114 |
| | | | WO 2002-US1130 | W 20020114 |

OTHER SOURCE(S): MARPAT 137:119644

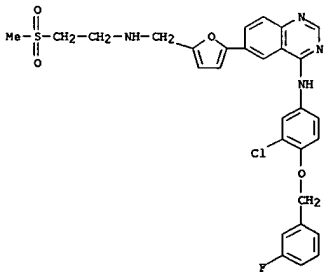
AB A method of treating **cancer** is described which includes administration of a 4-quinazolineamine (preparation included) and at least one other antineoplastic agent. Also described is a pharmaceutical combination including the 4-quinazolineamines.

IT **231277-92-2P**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(quinazolineamine derivative combination with other antineoplastic agent for **cancer** treatment, and compound preparation)

RN 231277-92-2 CAPLUS

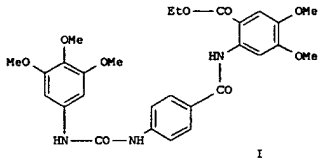
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 62 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)




L5 ANSWER 63 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:251274 CAPLUS
DOCUMENT NUMBER: 137:257225
TITLE: Synthesis and structure-activity relationship of diarylamide urea derivatives as selective inhibitors of the **proliferation** of human coronary artery smooth muscle cells
AUTHOR(S): Ogita, Haruhisa; Isobe, Yoshiaki; Takaku, Haruo; Sekine, Rena; Goto, Yuso; Misawa, Satoru; Hayashi, Hideya
CORPORATE SOURCE: Pharmaceuticals & Biotechnology Laboratory, Japan Energy Corporation, Toda-shi, Saitama, 335-8502, Japan
SOURCE: Bioorganic & Medicinal Chemistry (2002), 10(6), 1865-1871
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:257225
GI

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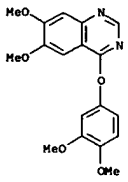
AB A series of diarylamide urea derivs. were synthesized and evaluated for their inhibitory activities against human coronary artery smooth muscle cells (SMCs) and human coronary artery endothelial cells (ECs). Compound I was superior to the lead compound, Tranilast, in terms of its potency of inhibitory activity and cell selectivity.

IT **202917-09-7**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(diarylamide urea derivs. as inhibitors of coronary artery smooth muscle cell **proliferation**)

RN 202917-09-7 CAPLUS

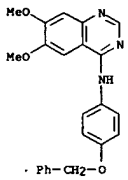
CN Quinazoline, 4-(3,4-dimethoxyphenoxy)-6,7-dimethoxy- (9CI) (CA INDEX NAME)

L5 ANSWER 63 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 64 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 64 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:79813 CAPLUS
DOCUMENT NUMBER: 136:363253
TITLE: Comparison of the biochemical and kinetic properties of the type 1 receptor tyrosine kinase intracellular domains: demonstration of differential sensitivity to kinase inhibitors
AUTHOR(S): Brignola, Perry S.; Lackey, Karen; Kadwell, Sue H.; Hoffman, Christine; Horne, Earnest; Carter, H. Luke; Stuart, J. Darren; Blackburn, Kevin; Moyer, Mary B.; Alligood, Krystal J.; Knight, Wilson B.; Wood, Edgar R.
CORPORATE SOURCE: Departments of Gene Expression and Protein Biochemistry, GlaxoSmithKline Inc., Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Biological Chemistry (2002), 277(2), 1576-1585
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Epidermal growth factor receptor (EGFR), ErbB-2, and ErbB-4 are members of the type 1 receptor tyrosine kinase family. Overexpression of these receptors, especially ErbB-2 and EGFR, has been implicated in multiple forms of cancer. Inhibitors of EGFR tyrosine kinase activity are being evaluated clin. for cancer therapy. The potency and selectivity of these inhibitors may affect the efficacy and toxicity of therapy. Here the authors describe the expression, purification, and biochem. comparison of EGFR, ErbB-2, and ErbB-4 intracellular domains. Despite their high degree of sequence homol., the three enzymes have significantly different catalytic properties and substrate kinetics. For example, the catalytic activity of ErbB-2 is less stable than that of EGFR. ErbB-2 uses ATP-Mg as a substrate inefficiently compared with EGFR and ErbB-4. The three enzymes have very similar substrate preferences for three optimized peptide substrates, but differences in substrate synergies were observed The authors have used the biochem. and kinetic parameters determined from these studies to develop an assay system that accurately measures inhibitor potency and selectivity between the type 1 receptor family. The authors report that the selectivity profile of mols. in the 4-anilinoquinazoline series can be modified through specific aniline substitutions. Moreover, these compds. have activity in whole cells that reflect the potency and selectivity of target inhibition determined with this assay system.

IT **179248-61-4**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(comparison of biochem. and kinetics of type 1 receptor tyrosine kinase intracellular domains and demonstration of differential sensitivity to kinase inhibitors in relation to anticancer activity)

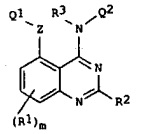
RN 179248-61-4 CAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-N-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 65 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:904160 CAPLUS
DOCUMENT NUMBER: 136:20087
TITLE: Preparation of 4-anilinoquinazoline derivatives for the treatment of tumors
INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited
SOURCE: PCT Int. Appl., 234 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2001094341 | A1 | 20011213 | WO 2001-GB2424 | | 20010601 |
| WO 2001094341 | C2 | 20030417 | | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | | |
| CA 2407371 | AA | 20011213 | CA 2001-2407371 | | 20010601 |
| EP 1292594 | A1 | 20030319 | EP 2001-934176 | | 20010601 |
| EP 1292594 | B1 | 20040901 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | | |
| BR 2001011335 | A | 20030610 | BR 2001-11335 | | 20010601 |
| JP 2003535859 | T2 | 20031202 | JP 2002-501890 | | 20010601 |
| EE 200200673 | A | 20040615 | EE 2002-673 | | 20010601 |
| NZ 522204 | A | 20040730 | NZ 2001-522204 | | 20010601 |
| AT 275145 | E | 20040915 | AT 2001-934176 | | 20010601 |
| US 2004214841 | A1 | 20041028 | US 2002-275382 | | 20021105 |
| ZA 2002009122 | A | 20040209 | ZA 2002-9122 | | 20021108 |
| BG 107332 | A | 20030731 | BG 2002-107332 | | 20021128 |
| NO 2002005792 | A | 20021202 | NO 2002-5792 | | 20021202 |
| PRIORITY APPLN. INFO.: | | | EP 2000-401581 | A | 20000606 |
| | | | EP 2001-400297 | A | 20010207 |
| | | | EP 2001-400565 | A | 20010305 |
| | | | WO 2001-GB2424 | W | 20010601 |

OTHER SOURCE(S): MARPAT 136:20087
GI



I

L5 ANSWER 65 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

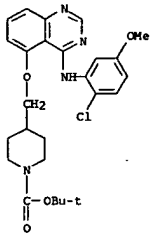
AB The invention concerns quinazoline derivs. (I; e.g. 4-(2-chloro-5-methoxyanilino)-7-methoxy-5-(3-morpholinopropoxy)quinazoline (1)), processes for their preparation, pharmaceutical compns. containing them and their use in the manufacture of a medicament for use as an anti-invasive agent in the containment and/or treatment of solid tumor disease. Although biol. assay methods are described, no test results are reported. It is believed that the antitumor activity is due to inhibition of one or more of the non-receptor tyrosine-specific protein kinases of the Src family that are involved in the signal transduction steps that lead to the invasiveness and migratory ability of metastasizing tumor cells. In I, according to the 1st claim, m = 0-3; each R1 = halo, trifluoromethyl, cyano, isocyano, nitro, hydroxy, mercapto, amino, formyl, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, (3-6C)alkenoylamino, N-(1-6C)alkyl-(3-6C)alkenoylamino, (3-6C)alkynoylamino, N-(1-6C)alkyl-(3-6C)alkynoylamino, N-(1-6C)alkylsulfamoyl, N,N-di[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, or Q3-X1- (X1 = direct bond, O, S, SO, SO2, N(R4), CO, CH(OR4), CON(R4), N(R4)CO, SO2N(R4), N(R4)SO2, OC(R4)2, SC(R4)2 and N(R4)C(R4)2 (R4 = H or (1-6C)alkyl) and Q3 = aryl, aryl-(1-6C)alkyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl-, (1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl), or (R1)m is (1-3C)alkylenedioxy, with addnl. optional substitution and/or insertion possible. R2 = H or (1-6C)alkyl; R3 = H or (1-6C)alkyl; Z = direct bond, O, S, SO, SO2, N(R11), CO, CH(OR11), CON(R11), N(R11)CO, SO2N(R11), N(R11)SO2, OC(R11)2, SC(R11)2 and N(R11)C(R11)2 (R11 = H, or (1-6C)alkyl). Q1 = aryl, aryl-(1-6C)alkyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl, or, when Z is a direct bond or O, Q1 may be (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, halo-(1-6C)alkyl, hydroxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl, di[(1-6C)alkyl]amino-(1-6C)alkyl, (1-6C)alkylthio-(1-6C)alkyl, (1-6C)alkylsulfinyl-(1-6C)alkyl or (1-6C)alkylsulfonyl-(1-6C)alkyl, with addnl. optional substitution and/or insertion possible. Q2 = substituted Ph. More than 50 example prepns. are included. For example, 1 was obtained by adding di-tert-Bu azodicarboxylate (0.208 g) dropwise to a stirred mixture of 4-(2-chloro-5-methoxyanilino)-5-hydroxy-7-methoxyquinazoline (0.2 g), 4-(3-hydroxypropyl)morpholine, PPh3 (0.237 g) and CH2Cl2 (3 mL). The reaction mixture was stirred at ambient temperature for 1 h.

IT **379228-73-6P**, 5-((N-(tert-Butoxycarbonyl)piperidin-4-yl)methoxy)-4-(2-chloro-5-methoxyanilino)quinazoline
RL: PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(intermediate; preparation of anilinoquinazoline derivs. for treatment of tumors)

RN 379228-73-6 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[[4-[(2-chloro-5-methoxyphenyl)amino]-5-

L5 ANSWER 65 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
quinazolinyl]oxy]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

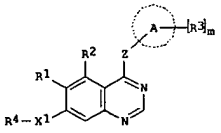
L5 ANSWER 66 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:762976 CAPLUS
DOCUMENT NUMBER: 135:303906
TITLE: Preparation of quinazolines useful in the production of an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal
INVENTOR(S): Hennequin, Laurent Francois Andre; Stokes, Elaine Sophie Elizabeth
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

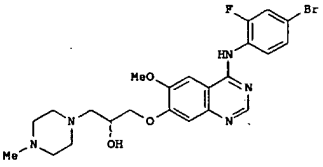
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001077085 | A1 | 20011018 | WO 2001-GB1514 | 20010403 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2403365 | AA | 20011018 | CA 2001-2403365 | 20010403 |
| BR 2001009828 | A | 20021217 | BR 2001-9828 | 20010403 |
| EP 1274692 | A1 | 20030115 | EP 2001-921530 | 20010403 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2003530387 | T2 | 20031014 | JP 2001-575560 | 20010403 |
| NZ 521421 | A | 20040924 | NZ 2001-521421 | 20010403 |
| ZA 2002007382 | A | 20031215 | ZA 2002-7382 | 20020913 |
| NO 2002004763 | A | 20021119 | NO 2002-4763 | 20021003 |
| US 2003191308 | A1 | 20031009 | US 2002-240658 | 20021003 |
| PRIORITY APPLN. INFO.: | | | EP 2000-400967 A | 20000407 |
| | | | EP 2000-400968 A | 20000407 |
| | | | EP 2000-401033 A | 20000413 |
| | | | EP 2000-401034 A | 20000413 |
| | | | WO 2001-GB1514 W | 20010403 |

OTHER SOURCE(S): MARPAT 135:303906
GI

L5 ANSWER 66 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



I



II

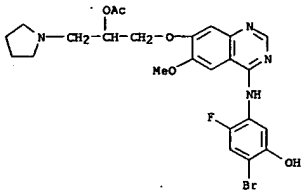
AB The title compds. [I; ring A = Ph, 5-6 membered heterocyclic ring; Z = O, NH, S; m = 0-5; R1 = H, OH, halo, etc.; R2 = H, OH, halo, etc.; R3 = OH, halo, alkyl, etc.; provided that when ring A = 5-6 membered heterocyclic ring, at least one R3 is either OH or halo; X1 = O, CH2, S, etc.; R4 = is selected from a number of groups defined herein comprising an alkylene, alkenylene or alkynylene chain wherein each methylene group (other than that of the α-carbon) is optionally substituted by 1 substituent independently selected from OH, halo, NH2 and alkanoyloxy], useful in disease states such as cancer, rheumatoid arthritis and psoriasis, were prepared and formulated. E.g., a multi-step synthesis of the quinazoline II which showed IC50 of 0.015-0.05 μM against the tyrosine kinase activity associated with VEGF receptor (KDR; in vitro), was given.

IT **367271-78-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of quinazolines useful in the production of an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal)

RN 367271-78-1 CAPLUS

CN 1-Pyrrolidineethanol, α-[[[4-[(4-bromo-2-fluoro-5-hydroxyphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-, monoacetate (ester) (9CI) (CA INDEX NAME)

L5 ANSWER 66 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 67 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

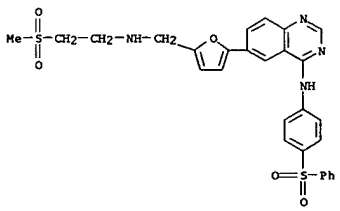
ACCESSION NUMBER: 2001:743253 CAPLUS
DOCUMENT NUMBER: 136:79264
TITLE: The characterization of novel, dual ErbB-2/EGFR, tyrosine kinase inhibitors: potential therapy for **cancer**
AUTHOR(S): Rusnak, David W.; Affleck, Karen; Cockerill, Stuart G.; Stubberfield, Colin; Harris, Robert; Page, Martin; Smith, Kathryn J.; Guntrip, Stephen B.; Carter, Malcolm C.; Shaw, Robert J.; Jowett, Amanda; Stables, Jeremy; Topley, Peter; Wood, Edgar R.; Brignola, Perry S.; Kadwell, Sue H.; Reep, Bryan R.; Mullin, Robert J.; Alligood, Krystal J.; Keith, Barry R.; Crosby, Renae M.; Murray, Doris M.; Knight, W. Blaine; Gilmer, Tona M.; Lackey, Karen
CORPORATE SOURCE: Department of Cancer Biology, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Cancer Research (2001), 61(19), 7196-7203
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The type 1 receptor tyrosine kinases constitute a family of transmembrane proteins involved in various aspects of cell growth and survival and have been implicated in the initiation and progression of several types of human malignancies. The best characterized of these proteins are the epidermal growth factor receptor (EGFR) and ErbB-2 (HER-2/neu). We have developed potent quinazoline and pyrido-[3,4-d]-pyrimidine small mols. that are dual inhibitors of ErbB-2 and EGFR. The compds. demonstrate potent in vitro inhibition of the ErbB-2 and EGFR kinase domains with IC50s <80 nM. Growth of ErbB-2- and EGFR-expressing **tumor** cell lines is inhibited at concns. <0.5 μM. Selectivity for **tumor** cell growth inhibition vs. normal human fibroblast growth inhibition ranges from 10- to >75-fold. **Tumor** growth in mouse s.c. xenograft models of the BT474 and HN5 cell lines is inhibited in a dose-responsive manner using oral doses of 10 and 30 mg/kg twice per day. In addition, the tested compds. caused a reduction of ErbB-2 and EGFR autophosphorylation in **tumor** fragments from these xenograft models. These data indicate that these compds. have potential use as therapy in the broad population of **cancer** patients overexpressing ErbB-2 and/or EGFR.

IT **386744-56-5**, GW 9525
RL: PAC (Pharmacological activity); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(characterization of novel, dual ErbB-2/EGFR, tyrosine kinase inhibitors and potential therapy for **cancer**)

RN 386744-56-5 CAPLUS
CN 4-Quinazolinamine, 6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-N-[4-(phenylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 67 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 68 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:545724 CAPLUS
DOCUMENT NUMBER: 135:147398
TITLE: Peptidomimetic modulators of cell adhesion
INVENTOR(S): Gour, Barbara J.; Blaschuk, Orest W.; Ali, Anmar; Ni, Feng; Chen, Zhigang; Michaud, Stephanie Denise; Wang, Shoameng; Hu, Zengjian
PATENT ASSIGNEE(S): Adherex Technologies, Inc., Can.
SOURCE: PCT Int. Appl., 416 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001053331 | A2 | 20010726 | WO 2001-US2508 | 20010124 |
| WO 2001053331 | A3 | 20020711 | | |
| WO 2001053331 | C2 | 20021031 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

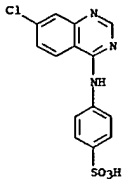
PRIORITY APPLN. INFO.: US 2000-491078 A 20000124
OTHER SOURCE(S): MARPAT 135:147398

AB Peptidomimetics of cyclic peptides, and compns. comprising such peptidomimetics are provided. The peptidomimetics have a three-dimensional structure that is substantially similar to a three-dimensional structure of a cyclic peptide that comprises a cadherin cell adhesion recognition sequence HAV. Methods for using such peptidomimetics for modulating cadherin-mediated cell adhesion in a variety of contexts are also provided.

IT **105037-36-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(peptidomimetic modulators of cell adhesion)

RN 105037-36-3 CAPLUS
CN Benzenesulfonic acid, 4-[(7-chloro-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 68 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L5 ANSWER 69 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:380561 CAPLUS
DOCUMENT NUMBER: 134:366897
TITLE: Preparation and pharmaceutical use of 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline to prevent the development of colorectal cancer
INVENTOR(S): Uckun, Fatih M.
PATENT ASSIGNEE(S): Parker Hughes Institute, USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001036394 | A1 | 20010525 | WO 2000-US31188 | 20001114 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2391396 | AA | 20010525 | CA 2000-2391396 | 20001114 |
| EP 1232146 | A1 | 20020821 | EP 2000-977201 | 20001114 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2003514803 | T2 | 20030422 | JP 2001-538883 | 20001114 |
| US 6482828 | B2 | 20021119 | US 2002-145639 | 20020514 |
| US 2002183340 | A1 | 20021205 | | |

PRIORITY APPLN. INFO.: US 1999-165499P P 19991115
WO 2000-US31188 W 20001114

AB Preventing the development or recurrence of colorectal cancer in a mammal comprising administering an effective cancer-preventive amount of 4-(4'-hydroxyphenyl)-amino-6,7-dimethoxyquinazoline (m.p. 245.0-248.0°; prepared in seven steps from 3,4-dimethoxy-6-nitrobenzoic acid) or a pharmaceutically acceptable salt.

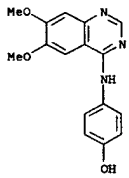
IT **340176-69-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); TEM (Technical or engineered material use); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and pharmaceutical use of 4-(4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline and its salts to prevent the development of colorectal cancer)

RN 340176-69-4 CAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]-, 4-methylbenzenesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

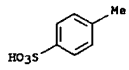
CRN 202475-60-3

L5 ANSWER 69 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
CMF C16 H15 N3 O3



CM 2

CRN 104-15-4
CMF C7 H8 O3 S



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 70 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:380393 CAPLUS
DOCUMENT NUMBER: 134:363426
TITLE: Radiosensitization of human glioblastoma cells by quinazoline compounds
INVENTOR(S): Uckun, Fatih M.; Narla, Rama K.
PATENT ASSIGNEE(S): Parker Hughes Institute, USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

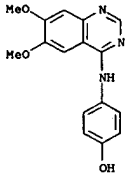
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001035952 | A2 | 20010525 | WO 2000-US31287 | 20001114 |
| W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: US 1999-165488P P 19991115
OTHER SOURCE(S): MARPAT 134:363426

AB The present invention is directed to a method of sensitizing cancer cells to radiation treatment by subjecting the cells to suitable quinazoline derivs., such as 4-(3'-bromo-4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline, or its pharmaceutically acceptable salt. The present invention is further directed to a cancer treatment, which includes a combination of (a) radiation and (b) a radiation-sensitizing amount of a suitable quinazoline deriv. or its pharmaceutically acceptable salt.

IT **202475-60-3P, WHI-P131**
RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(radiosensitization of human glioblastoma cells by quinazoline compds.)

RN 202475-60-3 CAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



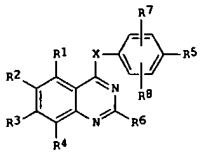
L5 ANSWER 71 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:228866 CAPLUS
DOCUMENT NUMBER: 134:266317
TITLE: Preparation of quinazolines as **aurora** 2 kinase inhibitors
INVENTOR(S): Mortlock, Andrew Austen; Keen, Nicholas John; Jung, Frederic Henri; Brewster, Andrew George
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 306 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001021596 | A1 | 20010329 | WO 2000-GB3580 | 20000918 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2384291 | AA | 20010329 | CA 2000-2384291 | 20000918 |
| BR 2000014116 | A | 20020521 | BR 2000-14116 | 20000918 |
| EP 1218354 | A1 | 20020703 | EP 2000-960840 | 20000918 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2003509499 | T2 | 20030311 | JP 2001-524975 | 20000918 |
| EE 200200119 | A | 20030415 | EE 2002-119 | 20000918 |
| BG 106492 | A | 20030131 | BG 2002-106492 | 20020307 |
| ZA 2002002234 | A | 20030619 | ZA 2002-2234 | 20020319 |
| NO 2002001399 | A | 20020430 | NO 2002-1399 | 20020320 |

PRIORITY APPLN. INFO.:
GB 1999-22154 A 19990921
GB 1999-22170 A 19990921
WO 2000-GB3580 W 20000918

OTHER SOURCE(S): MARPAT 134:266317
GI

L5 ANSWER 71 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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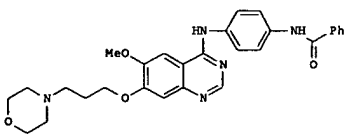
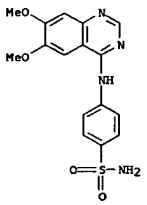


II

AB Title compds. (I) [wherein X = O, S, SO, SO2, NH, or NR12; R12 = H or alkyl; R1-R4 = independently halo, CN, NO2, alkylsulfanyl, N(OH)R13, or R15X1; R13 = H or alkyl; X1 = a direct bond, O, CH2, OC(O), CO, CO2, S, SO, SO2, or (un)substituted NHCO, CONH, SO2NH, NHSO2, or NH; R15 = H or (un)substituted hydrocarbyl, heterocyclyl, or alkoxy; R5 = NHCO2R9, NHCOR9, NHSO2R9, COR9, CO2R9, SOR9, SO2OR9, CONR10R11, SONR10R11, or SO2NR10R11; R9-R11 = independently H or (un)substituted hydrocarbyl or heterocyclyl; or R10 and R11 together with the N to which they are attached = (un)substituted heterocyclyl; R6 = H or (un)substituted hydrocarbyl or heterocyclyl; R7 and R8 = independently H, halo, alkyl, (di)alkoxy(methyl), alkanoyl, CF3, CN, NHY2, alkenyl, alkynyl, or (un)substituted Ph, PhCH2, or heterocyclyl; or a salt, ester, or amide thereof] were prepared as **aurora** 2 kinase inhibitors for the treatment of **proliferative** diseases, such as **cancer**. For example, a 7-step sequence involving (1) alkylation of morpholine with 1-bromo-3-chloropropane (49%), (2) addition of Et vanillate to yield Et 3-methoxy-4-(3-morpholinopropoxy)benzoate (100%), (3) nitration (86%), (4) reduction to the amine using 10% Pd/C (100%), (5) cycloaddn. with formamide to form the quinazoline(68%), (6) chlorination to give 4-chloro-6-methoxy-7-(3-morpholinopropoxy)quinazoline (60%), and (7) amination with N-benzoyl-4-aminoaniline (58%) yielded II. The latter inhibited the serine/threonine kinase activity of **aurora** 2 kinase by 50% at a concentration of 0.0193 μM. In addition, II gave 50% inhibition of MCF-7 cell **proliferation** at 1.06 μM and reduced BrdU incorporation into cellular DNA by 50% at 0.159-0.209 μM.

IT **202475-67-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-substituted quinazoline **aurora** 2 kinase

L5 ANSWER 71 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
inhibitors for treatment of **cancer** and other **proliferative** diseases)
RN 202475-67-0 CAPLUS
CN Benzenesulfonamide, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 72 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:228864 CAPLUS
DOCUMENT NUMBER: 134:252355
TITLE: Preparation of quinazolines as **aurora** 2 kinase inhibitors
INVENTOR(S): Mortlock, Andrew Austen; Keen, Nicholas John
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001021594 | A1 | 20010329 | WO 2000-GB3556 | 20000918 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2384282 | AA | 20010329 | CA 2000-2384282 | 20000918 |
| BR 2000014133 | A | 20020611 | BR 2000-14133 | 20000918 |
| TR 200200749 | T2 | 20020621 | TR 2002-200200749 | 20000918 |
| EP 1218356 | A1 | 20020703 | EP 2000-962677 | 20000918 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2003509497 | T2 | 20030311 | JP 2001-524973 | 20000918 |
| EE 200200149 | A | 20030415 | EE 2002-149 | 20000918 |
| AU 763242 | B2 | 20030717 | AU 2000-74325 | 20000918 |
| ZA 2002001833 | A | 20030605 | ZA 2002-1833 | 20020305 |
| BG 106491 | A | 20021229 | BG 2002-106491 | 20020307 |
| NO 2002001401 | A | 20020521 | NO 2002-1401 | 20020320 |

PRIORITY APPLN. INFO.:
GB 1999-22152 A 19990921
GB 1999-22156 A 19990921
GB 1999-22159 A 19990921
WO 2000-GB3556 W 20000918

OTHER SOURCE(S): MARPAT 134:252355
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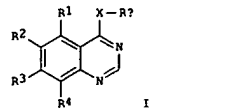
L5 ANSWER 72 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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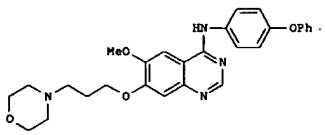


II

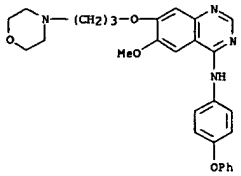
AB Title compds. (I) [wherein X = O, S, SO, SO2, NH, or NR8; R8 = H or alkyl; Ra = (un)substituted 3-quinolinyl or Ph; R1-R4 = independently halo, CN, NO2, alkylsulfanyl, N(OH)R12, or R14X1; R12 = H or alkyl; X1 = a direct bond, O, CH2, OC(O), CO, S, SO, SO2, or (un)substituted NHCO, CONH, SO2NH, NHSO2, or NH; R14 = H or (un)substituted hydrocarbyl, heterocyclyl, or alkoxy; or a salt, ester, or amide thereof] were prepared as **aurora** 2 kinase inhibitors for the treatment of **proliferative** diseases, such as **cancer**. For example, 4-phenoxyaniline•HCl and 4-chloro-6-methoxy-7-(3-morpholinopropoxy)quinazoline were refluxed in i-PrOH to yield II (86%). The latter inhibited the serine/threonine kinase activity of **aurora** 2 kinase by 50% at a concentration of 0.069 μM. In addition, II gave 50% inhibition of MCF-7 cell **proliferation** at 2.89 μM and reduced BrdU incorporation into cellular DNA by 50% at 3.68 μM.

IT **330999-53-6P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-substituted quinazoline **aurora** 2 kinase inhibitors by coupling quinolinyl or Ph alcs., thiols, or amines with 4-haloquinazolines)

RN 330999-53-6 CAPLUS

CN 4-Quinazolinamine, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-N-(4-phenoxyphenyl)- (9CI) (CA INDEX NAME)

L5 ANSWER 72 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 73 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:50639 CAPLUS
DOCUMENT NUMBER: 134:100886
TITLE: Preparation of anilinoquinazolines as protein tyrosine kinase inhibitors
INVENTOR(S): Cockerill, George Stuart; Lackey, Karen Elizabeth
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001004111 | A1 | 20010118 | WO 2000-US18128 | 20000630 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1192151 | A1 | 20020403 | EP 2000-943348 | 20000630 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2003504363 | T2 | 20030204 | JP 2001-509721 | 20000630 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| GB 1999-16213 | A | 19990709 |
| GB 1999-16218 | A | 19990709 |
| WO 2000-US18128 | W | 20000630 |

OTHER SOURCE(S): MARPAT 134:100886
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

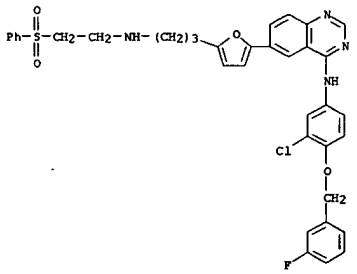
AB The title compds. [I; X = CR1 and Y = N; or X = N and Y = CR1; X = CR1 and Y = CR2; X = CR2 and Y = CR1; R1 = Ar(CH2)pZCH2CH2SO2R5 (wherein Ar = (un)substituted Ph, furan, thiophene, etc.; Z = O, S, NH, NR6; p = 1-4; R5 = alkyl substituted by 5-10 membered heterocyclic group, 3-10 membered carbocyclic group, etc.; R6 = alkyl, alkoxyalkyl, hydroxyalkyl, etc.); R2 = H, halo, OH, etc.; R3 = pyridylmethoxy, benzyloxy, halo-, dihalo- and trihalobenzyloxy; R4 = H, halo, alkyl, etc.; with the proviso that when p = 1 and Z = NH, R5 cannot represent Me] which exhibit protein tyrosine kinase inhibition, in particular erbB family kinase inhibition, and useful in treating **cancer** and psoriasis, were prepared E.g., a multi-step synthesis of the anilinoquinazoline II was given. Biol. data (erbB-2, erbB-4, EGFr, and cell **proliferation** inhibition) for the compds. I were presented.

IT **319917-32-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of anilinoquinazolines as protein tyrosine kinase inhibitors)

RN 319917-32-3 CAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[3-

L5 ANSWER 73 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
[[2-(phenylsulfonyl)ethyl]amino]propyl]-2-furanyl]- (9CI) (CA INDEX NAME)

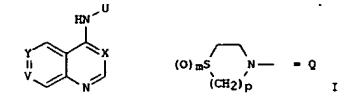


REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 74 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:854415 CAPLUS
DOCUMENT NUMBER: 133:362769
TITLE: Preparation of 6-(thiomorpholinomethylfuranyl)-4-quinazolinamines as protein tyrosine kinase inhibitors
INVENTOR(S): Carter, Malcolm Clive; Cockerill, George Stuart; Guntrip, Stephen Barry; Lackey, Karen Elizabeth; Smith, Kathryn Jane
PATENT ASSIGNEE(S): Glaxo Group Ltd., UK
SOURCE: Brit. UK Pat. Appl., 151 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| GB 2345486 | A1 | 20000712 | GB 1999-29973 | 19991217 |
| PRIORITY APPLN. INFO.: | | | GB 1999-518 A | 19990111 |
| | | | GB 1999-15510 A | 19990703 |

OTHER SOURCE(S): MARPAT 133:362769
GI



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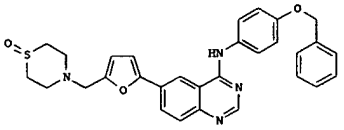
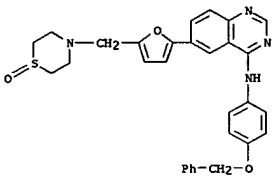


II

AB The title compds. (I) [wherein X = N or CH; V and Y = independently CR1, CR2, or N; and V ≠ Y; R1 = Q(CH2)qAr; m = 1 or 2; p = 1 or 2; q = 1-4; Ar = (un)substituted Ph, furanyl, thiophenyl, pyrrolyl, or thiazolyl; R2 = H, halo, OH, alkyl(amino) alkoxy, or dialkylamino; U = (un)substituted Ph, pyridyl, (benz)imidazolyl, (iso)indolyl, (iso)indolinyl, indazolyl, or benzotriazolyl] were prepared as protein tyrosine kinase inhibitors for the treatment of cancer and other disorders mediated by aberrant protein tyrosine kinase activity. For example, II•2HCl was formed in a multi-step sequence involving (1)

L5 ANSWER 74 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
reaction of 5-(1,3-dioxolan-2-yl)-2-(tributylstannyl)furan with (4-benzyloxyphenyl)(6-bromoquinazolin-4-yl)amine using Pd(PPh3)2Cl2 in dioxane, (2) conversion of the cyclic acetal to the aldehyde with HCl in THF, (3) addn. of thiomorpholine-S-oxide in CH2Cl2 and conversion to the HCl salt. I inhibited EGFR and c-erbB-2 tyrosine kinase with IC50 < 0.10 μM and suppressed cell proliferation against a range of tumor cell lines.
IT 307328-02-5P, (4-Benzyloxyphenyl)-[6-[5-(1-oxothiomorpholin-4-ylmethyl)furan-2-yl]quinazolin-4-yl]amine dihydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of thiomorpholinomethylfuranyl quinazolinamine and pyrido[3,4-d]pyrimidinamine anticancer agents by amination of (haloheterocyclyl)furancarboxaldehydes with anilines followed by addition of thiomorpholine (oxides))
RN 307328-02-5 CAPLUS
CN 4-Quinazolinamine, 6-[5-[(1-oxido-4-thiomorpholinyl)methyl]-2-furanyl]-N-[4-(phenylmethoxy)phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)

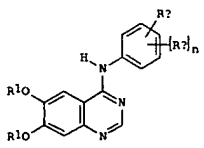


●2 HCl

L5 ANSWER 75 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:688226 CAPLUS
DOCUMENT NUMBER: 133:266866
TITLE: Preparation of quinazolines as antitumor agents
INVENTOR(S): Uckun, Fatih M.; Liu, Xing-ping; Narla, Rama K.
PATENT ASSIGNEE(S): Parker Hughes Institute, USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

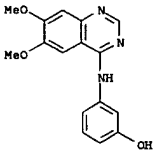
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000056720 | A1 | 20000928 | WO 2000-US6902 | 20000316 |
| W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6258820 | B1 | 20010710 | US 1999-357404 | 19990720 |
| CA 2367861 | AA | 20000928 | CA 2000-2367861 | 20000316 |
| EP 1163228 | A1 | 20011219 | EP 2000-921389 | 20000316 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002540103 | T2 | 20021126 | JP 2000-606581 | 20000316 |
| US 2001016588 | A1 | 20010823 | US 2001-779809 | 20010208 |
| US 6358962 | B2 | 20020319 | | |
| US 2002137757 | A1 | 20020926 | US 2001-923903 | 20010807 |
| US 6638939 | B2 | 20031028 | | |
| NO 2001004560 | A | 20010919 | NO 2001-4560 | 20010919 |
| US 2004039002 | A1 | 20040226 | US 2003-454960 | 20030605 |
| PRIORITY APPLN. INFO.: | | | US 1999-125145P P | 19990319 |
| | | | US 1999-125177P P | 19990319 |
| | | | US 1999-125338P P | 19990319 |
| | | | US 1999-357404 A | 19990720 |
| | | | WO 2000-US6902 W | 20000316 |
| | | | US 2001-779809 A1 | 20010208 |
| | | | US 2001-923903 A1 | 20010807 |

OTHER SOURCE(S): MARPAT 133:266866
GI



I

L5 ANSWER 75 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
AB The title compds. [I; Ra = I, hydroxyalkyl, methylenedioxy, etc.; n = 1-4; Rb = H, halo, OH, etc.; R1 = alkyl], useful for the treatment of cancer (e.g., leukemia and breast cancer) and for the treatment of allergic reactions, were prepared by reacting 4-chloro-6,7-dimethoxyquinazoline with the substituted aniline. Biol. data for compds. I were given.
IT 153437-55-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazolines as antitumor agents)
RN 153437-55-9 CAPLUS
CN Phenol, 3-[(6,7-dimethoxy-4-quinazolinyl)amino]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

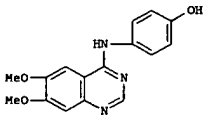
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 76 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:688094 CAPLUS
DOCUMENT NUMBER: 133:271682
TITLE: Preparation of quinazolines for micellar pharmaceuticals for treatment of allergy and cancer
INVENTOR(S): Yiv, Seang; Li, Mingshu; Uckun, Fatih M.
PATENT ASSIGNEE(S): Parker Hughes Institute, USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000056338 | A1 | 20000928 | WO 2000-US7066 | 20000317 |
| W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2366998 | AA | 20000928 | CA 2000-2366998 | 20000317 |
| EP 1162974 | A1 | 20011219 | EP 2000-914991 | 20000317 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002539262 | T2 | 20021119 | JP 2000-606242 | 20000317 |
| US 2002111360 | A1 | 20020815 | US 2001-960464 | 20010919 |

PRIORITY APPLN. INFO.: US 1999-125147P P 19990319
WO 2000-US7066 W 20000317

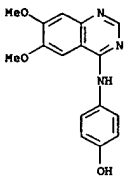
OTHER SOURCE(S): MARPAT 133:271682
GI



I

AB Pharmaceutical compns. for parenteral administration of poorly soluble quinazoline compds. in the form of microemulsions or micellar solns. are described. The compns. are useful in treating patients suffering from cancer or having allergic reactions. E.g., I was prepared, its soly profile given, and micellar solns. containing PEGylated phosphatidylethanolamines were effective in enhancing the solubilization

L5 ANSWER 76 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
of I.
IT 202475-60-3P
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of quinazolines for micellar pharmaceuticals for treatment of allergy and cancer)
RN 202475-60-3 CAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



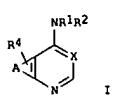
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 77 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:592396 CAPLUS
DOCUMENT NUMBER: 133:193157
TITLE: Preparation of aminoquinazolines and related compounds as anticancer drugs.
INVENTOR(S): Kath, John Charles; Tom, Norma Jacqueline; Cox, Eric David; Bhattacharya, Samit Kumar
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 39 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 1029853 | A1 | 20000823 | EP 1999-310574 | 19991224 |
| EP 1029853 | B1 | 20040225 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2000309577 | A2 | 20001107 | JP 1999-336570 | 19991126 |
| JP 3270834 | B2 | 20020402 | | |
| CA 2290918 | AA | 20000727 | CA 2000-2290918 | 19991129 |
| CA 2290918 | C | 20040217 | CA 1999-2290918 | 19991129 |
| EP 1396489 | A1 | 20040310 | EP 2003-24331 | 19991224 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY | | | | |
| AT 260263 | E | 20040315 | AT 1999-310574 | 19991224 |
| PT 1029853 | T | 20040531 | PT 1999-310574 | 19991224 |
| ES 2214820 | T3 | 20040916 | ES 1999-310574 | 19991224 |
| BR 9906013 | A | 20000905 | BR 1999-6013 | 19991229 |
| US 6465449 | B1 | 20021015 | US 2000-488378 | 20000120 |
| US 2003055049 | A1 | 20030320 | US 2002-226255 | 20020822 |

PRIORITY APPLN. INFO.: US 1999-117341P P 19990127
EP 1999-310574 A3 19991224
US 2000-488378 A3 20000120

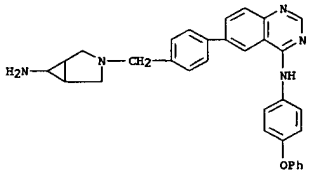
OTHER SOURCE(S): MARPAT 133:193157
GI



I

AB Title compds. [I; X = N, CH; A = (substituted) fused 5-7 membered ring optionally containing 1-4 heteroatoms selected from NR1, O, S, SO, SO2 containing 1-3 double bonds inclusive of the bond in the pyridine or pyrimidine ring to which it is fused etc.; R1 = H, alkyl; R3 = (CR1R2)mR8; m = 0, 1; R1R3N = (substituted) 1-indolinyl, 1-indolyl; R4, R8 = (substituted) aryl(alkyl), heterocyclyl(alkyl)], were prepared as neoplasm inhibitors (no data). Thus, 3-[4-(4-phenoxy-quinazolin-6-yl)benzyl]-3-aza-bicyclo[3.1.0]hex-6-ylmethanol (preparation given), 1-cyclopropylmethyl-1H-indol-5-ylamine, pyridinium hydrochloride, and phenol were heated at

L5 ANSWER 77 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
110° overnight to give 67% [3-{4-[4-(1-cyclopropylmethyl-1H-indol-5-ylamino)-quinazolin-6-yl]-benzyl}-3-azabicyclo[3.1.0]hex-6-yl]methanol.
IT 289036-76-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoquinazolines and related compds. as anticancer drugs)
RN 289036-76-6 CAPLUS
CN 3-Azabicyclo[3.1.0]hexan-6-amine, 3-[[4-[4-[(4-phenoxyphenyl)amino]-6-quinazolinyl]phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

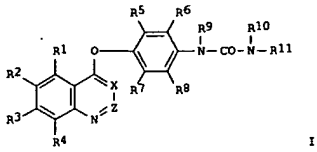
L5 ANSWER 78 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:513673 CAPLUS
DOCUMENT NUMBER: 133:135235
TITLE: Preparation and anti-tumor, anti-atherosclerosis, anti-psoriasis, anti-diabetes, and anti-arthritis activities of quinolines and quinazolines
INVENTOR(S): Kubo, Kazuo; Fujiwara, Yasunari; Isoe, Toshiyuki
PATENT ASSIGNEE(S): Kirin Beer Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 208 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000043366 | A1 | 20000727 | WO 2000-JP255 | 20000120 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2361057 | AA | 20000727 | CA 2000-2361057 | 20000120 |
| BR 2000007656 | A | 20011030 | BR 2000-7656 | 20000120 |
| EP 1153920 | A1 | 20011114 | EP 2000-900841 | 20000120 |
| EP 1153920 | B1 | 20031029 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| TR 200102090 | T2 | 20020121 | TR 2001-200102090 | 20000120 |
| JP 2003286263 | A2 | 20031010 | JP 2003-128216 | 20000120 |
| NZ 513006 | A | 20031031 | NZ 2000-513006 | 20000120 |
| AT 253051 | E | 20031115 | AT 2000-900841 | 20000120 |
| EP 1384712 | A1 | 20040128 | EP 2003-24911 | 20000120 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY | | | | |
| AU 771504 | B2 | 20040325 | AU 2000-30748 | 20000120 |
| JP 3519368 | B2 | 20040412 | JP 2000-594782 | 20000120 |
| ES 2208261 | T3 | 20040616 | ES 2000-900841 | 20000120 |
| NO 2001002617 | A | 20010914 | NO 2001-2617 | 20010529 |
| US 6797823 | B1 | 20040928 | US 2001-889858 | 20010723 |
| US 2004209905 | A1 | 20041021 | US 2004-842009 | 20040510 |

PRIORITY APPLN. INFO.:
JP 1999-14858 A 19990122
JP 1999-26691 A 19990203
JP 1999-142493 A 19990521
JP 1999-253624 A 19990907
EP 2000-900841 A3 20000120
JP 2000-594782 A3 20000120
WO 2000-JP255 W 20000120
US 2001-889858 A3 20010723

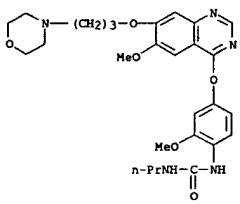
OTHER SOURCE(S): MARPAT 133:135235
GI

L5 ANSWER 78 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



I

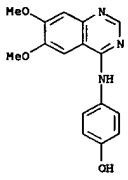
AB Title compds. [I; X and Z represent each CH or N; R1-3 represent each H, optionally substituted alkoxy, etc.; R4 represents H; R5-8 represent each H, halogeno, alkyl, alkoxy, alkylthio, nitro or amino, provided that all of R5-8 do not represent H simultaneously; R9 and R10 represent each H, alkyl or alkylcarbonyl; and R11 represents alkyl, alkenyl, alkynyl or aralkyl], pharmaceutically acceptable salts and solvates, and medicinal compns. containing the same are prepared and tested having antitumor activity and causing no morphol. change in cells. Thus, the title compound I (X = CH; Z = CH; R1, R4, R5,R7-R10 each an H; R11 = 3,5-F2C6H3) was prepared and tested.
IT 286371-28-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor activity of quinolines and quinazolines)
RN 286371-28-6 CAPLUS
CN Urea, N-[2-methoxy-4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]oxy]phenyl]-N'-propyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 79 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:228537 CAPLUS
DOCUMENT NUMBER: 132:342816
TITLE: Structure-based design of potent inhibitors of EGF-receptor tyrosine kinase as anti-cancer agents
AUTHOR(S): Ghosh, Sutapa; Narla, Rama Krishna; Zheng, Yaguo; Liu, Xing-Ping; Jun, Xiao; Mao, Chen; Sudbeck, Elise A.; Uckun, Fatih M.
CORPORATE SOURCE: Parker Hughes Cancer Center, Departments of Structural Biology, Parker Hughes Institute, St Paul, MN, 55113, USA
SOURCE: Anti-Cancer Drug Design (1999), 14(5), 403-410
CODEN: ACDDEA; ISSN: 0266-9536
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In a systematic effort to design inhibitors of the epidermal growth factor receptor (EGFR) family protein tyrosine kinases (PTK) as anti-cancer agents, we have constructed a three-dimensional homol. model of the EGFR kinase domain and used mol. modeling methods for the structure-based design of analogs of the active metabolite of leflunomide (LFM) with potent and specific inhibitory activity against EGFR. These docking studies identified α-cyano-β-hydroxy-β-methyl-N-[4-(trifluoromethoxy)phenyl]-p ropenamide (LFM-A12) as our lead compound, which was predicted to bind to the EGFR catalytic site in a planar conformation. LFM-A12 inhibited the proliferation (IC50 = 26.3 μM) and in vitro invasiveness (IC50=28.4 μM) of EGFR pos. human breast cancer cells in a concentration-dependent fashion. Similarly, the model of the EGFR binding pocket was used in combination with docking procedures to predict the favorable placement of chemical groups with defined sizes at multiple modification sites on another class of EGFR inhibitors, the 4-anilinoquinazoline. This approach has led to the successful design of a dibromo quinazoline derivative, WHI-P97, which had an estimated Ki value of 0.09 μM from modeling studies and a measured IC50 value of 2.5 μM in EGFR kinase inhibition assays. WHI-P97 effectively inhibited the in vitro invasiveness of EGFR-pos. human cancer cells in a concentration-dependent manner. However, unlike LFM-A12, the quinazoline compds. are not specific for EGFR.
IT 202475-60-3, WHI-P131
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure-based design of potent inhibitors of EGF-receptor tyrosine kinase as anti-cancer agents)
RN 202475-60-3 CAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 79 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 80 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:144864 CAPLUS
DOCUMENT NUMBER: 132:189690
TITLE: Therapeutic uses of quinazoline derivatives as JAK-3 kinase inhibitors
INVENTOR(S): Navara, Christopher S.; Mahajan, Sandeep; Uckun, Fatih M.
PATENT ASSIGNEE(S): Hughes Institute, USA
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000010981 | A1 | 20000302 | WO 1999-US19043 | 19990820 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2342503 | AA | 20000302 | CA 1999-2342503 | 19990820 |
| AU 9956827 | A1 | 20000314 | AU 1999-56827 | 19990820 |
| EP 1105378 | A1 | 20010613 | EP 1999-943800 | 19990820 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2002523403 | T2 | 20020730 | JP 2000-566255 | 19990820 |
| NO 2001000887 | A | 20010423 | NO 2001-887 | 20010221 |
| US 2002042513 | A1 | 20020411 | US 2001-858824 | 20010516 |
| US 6469013 | B2 | 20021022 | | |
| US 2004192711 | A1 | 20040930 | US 2003-715773 | 20031117 |

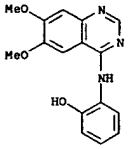
PRIORITY APPLN. INFO.: US 1998-97359P P 19980821
US 1998-97365P P 19980821
US 1999-378093 A3 19990820
WO 1999-US19043 W 19990820
US 2000-688756 A3 20001016

OTHER SOURCE(S): MARPAT 132:189690

AB The invention provides novel JAK-3 kinase inhibitors that are useful for treating leukemia and lymphoma. The compds. are also useful to treat or prevent skin **cancer**, as well as sunburn and UVB-induced skin inflammation. In addition, the compds. of the present invention prevent the immunosuppressive effects of UVB radiation, and are useful to treat or prevent autoimmune diseases, inflammation, and transplant rejection. The invention also provides pharmaceutical compns. comprising compds. of the invention, as well as therapeutic methods for their use. For example, treatments with 50 mg/kg or 75 mg/kg of a quinazoline derivative WHI-P131 (preparation given) were as effective as cyclosporin A treatment in prolongation of islet allograft survival in mice.

IT **211555-07-6P**, WHI-P 132
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); **THU**

L5 ANSWER 80 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
**(Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(WHI-P 132; therapeutic uses of quinazoline derivs. as JAK-3 kinase inhibitors)
RN 211555-07-6 CAPLUS
CN Phenol, 2-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



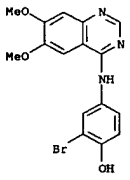
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 81 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:54949 CAPLUS
DOCUMENT NUMBER: 132:329420
TITLE: Specificity of α-cyano-β-hydroxy-β-methyl-N-[4-(trifluoromethoxy)phenyl]-p ropenamide as an inhibitor of the epidermal growth factor receptor tyrosine kinase
AUTHOR(S): Ghosh, Sutapa; Zheng, Yaguo; Jun, Xiao; Mahajan, Sandeep; Mao, Chen; Sudbeck, Elise A.; Uckun, Fatih M.
CORPORATE SOURCE: Parker Hughes Cancer Center, Departments of Structural Biology, Hughes Institute, St.Paul, MN, 55113, USA
SOURCE: Clinical Cancer Research (1999), 5(12), 4264-4272
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The epidermal growth factor receptor (EGFR) tyrosine kinase has an essential function for the survival of human breast **cancer** cells. In a systematic effort to design potent and specific inhibitors of this receptor family protein tyrosine kinase (PTK) as antibreast **cancer** agents, we recently reported the construction of a three-dimensional homol. model of the EGFR kinase domain. In this model, the catalytic site is defined by two β-sheets that form an interface at the cleft between the NH2-terminal and COOH-terminal lobes of the kinase domain. Our modeling studies revealed a distinct, remarkably planar triangular binding pocket within the kinase domain with approx. dimensions of 15 Å + 12Å + 12Å, and the thickness of the binding pocket is .apprx.7Å with an estimated volume of .apprx.600 Å3 available for inhibitor binding. Mol. docking studies had identified α-cyano-β-hydroxy-β-methyl-N-[4-(trifluoromethoxy)phenyl]-p ropenamide (LFM-A12) as our lead inhibitor, with an estimated binding constant of 13 μM, which subsequently inhibited EGFR kinase in vitro with an IC50 value of 1.7 μM. LFM-A12 was also discovered to be a highly specific inhibitor of the EGFR. Even at very high concns. ranging from 175-350 μM, this inhibitor did not affect the enzymic activity of other PTKs, including the Janus kinases JAK1 and JAK3, the Src family kinase HCK, the Tec family member Bruton's tyrosine kinase, SYK kinase, and the receptor family PTK insulin receptor kinase. This observation is in contrast to the activity of a quinazoline inhibitor tested as a control, 4-(3-bromo, 4-hydroxyanilino)-6,7-dimethoxyquinazoline, which was shown to inhibit EGFR and other tyrosine kinases such as HCK, JAK3, and SYK.

IT **211555-04-3**, WHI-P154
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(epidermal growth factor receptor tyrosine kinase inhibitor LFM-A12)
RN 211555-04-3 CAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 81 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 82 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:764027 CAPLUS
DOCUMENT NUMBER: 132:9009
TITLE: Quinazolines and conjugates thereof for treating brain tumors
INVENTOR(S): Uckun, Fatih M.; Narla, Rama K.; Liu, Xing-Ping
PATENT ASSIGNEE(S): Wayne Hughes Institute, USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9961428 | A1 | 19991202 | WO 1999-US11767 | 19990528 |
| W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2333392 | AA | 19991202 | CA 1999-2333392 | 19990528 |
| AU 9943173 | A1 | 19991213 | AU 1999-43173 | 19990528 |
| EP 1082311 | A1 | 20010314 | EP 1999-953336 | 19990528 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2002516823 | T2 | 20020611 | JP 2000-550834 | 19990528 |
| US 6316454 | B1 | 20011113 | US 1999-361088 | 19990726 |
| NO 2000005864 | A | 20010129 | NO 2000-5864 | 20001120 |
| US 2002161226 | A1 | 20021031 | US 2001-903294 | 20010711 |
| US 6552027 | B2 | 20030422 | | |

PRIORITY APPLN. INFO.:
US 1998-87479 A 19980529
WO 1999-US11767 W 19990528
US 1999-361088 A1 19990726

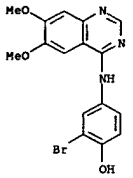
OTHER SOURCE(S): MARPAT 132:9009

AB Substituted quinazoline compds. and conjugates useful for inhibiting the growth of brain tumor cells and for inhibiting adhesion and migration of brain tumor cells are provided. The compds. include 4-(3'-bromo-4'-hydroxyphenyl)amino-6,7-dimethoxyquinazoline and this compound covalently bound to e.g. EGF.

IT 211555-04-3DP, WHI-P154, EGF conjugates
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); THU (Therapeutic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(quinazoline derivs., preparation, conjugates, and use for treating brain tumors)

RN 211555-04-3 CAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 82 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



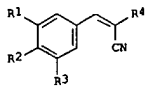
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

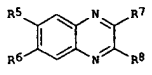
L5 ANSWER 83 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:718981 CAPLUS
DOCUMENT NUMBER: 131:322425
TITLE: Preparation of phenylacrylonitriles, quinoxalines, quinazolines, and related compounds as modulators of tyrosine kinase signal transduction
INVENTOR(S): App, Harald; McMahon, Gerald M.; Tang, Peng Cho; Gazit, Aviv; Levitzki, Alexander
PATENT ASSIGNEE(S): Yissum Research Development Company of the Hebrew University of Jerusalem, Israel; Sugen, Inc.
SOURCE: U.S., 21 pp., Cont.-in-part of U.S. 5,712,395.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

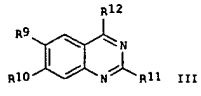
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5981569 | A | 19991109 | US 1995-463247 | 19950605 |
| CA 2149298 | AA | 19940526 | CA 1993-2149298 | 19931115 |
| EP 1378570 | A1 | 20040107 | EP 2003-9148 | 19931115 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| US 6177401 | B1 | 20010123 | US 1994-193829 | 19940209 |
| US 5712395 | A | 19980127 | US 1995-386021 | 19950209 |

PRIORITY APPLN. INFO.:
US 1992-975750 B2 19921113
US 1993-38596 B2 19930326
US 1994-193829 A2 19940209
US 1995-386021 A2 19950209
EP 1994-900810 A3 19931115

OTHER SOURCE(S): MARPAT 131:322425
GI


I


II

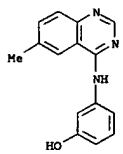

III

AB Title compds., e.g., [I, II, III; R1 = Me2CH, Me3C, iodo, Br, OH, Me; R2 = OH; R3 = Me2CH, Me3C, OH, H, Me; R4 = 1-phenyl-n-propylaminocarbonyl, (E)-1-cyano-2-[(3,5-diisopropyl-4-hydroxy)phenyl]ethenylsulfonyl, aminothiocarbonyl, cyanomethylsulfonyl, (3-amino-4-cyano)pyrazol-4-yl, etc.; R5, R6 = H, Me; R7 = H, CHO, Cl; R8 = Ph, 3,4-dihydroxyphenyl, 4-iodophenylamino, 3-chlorophenylamino, etc.; R9 = H, Me, OMe; R10 = H, OMe; R11 = H, Cl; R12 = 3-chlorophenylamino, 4-methylphenylmercapto,

L5 ANSWER 83 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
4-iodophenylamino, 3-hydroxyphenylamino], were prepd. as modulators of KDR/FLK-1 receptor signal transduction useful to regulate and/or modulate vasculogenesis and angiogenesis. Thus, 3,5-di-tert-butyl-4-hydroxybenzaldehyde, thiocyanoacetamide, and β-alanine were refluxed 6 h in EtOH to give (E)-2-aminothiocarbonyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl)acrylonitrile. The latter showed IC50 = 0.8 μM in an in vitro FLK-1R ELISA assay.

IT 168835-92-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylacrylonitriles and related compds. as modulators of tyrosine kinase signal transduction)

RN 168835-92-5 CAPLUS
CN Phenol, 3-[(6-methyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 84 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:451297 CAPLUS
DOCUMENT NUMBER: 131:102288
TITLE: Bicyclic heteroaromatic compounds [quinazolinamines, pyridopyrimidines, and analogs] useful as protein tyrosine kinase inhibitors
INVENTOR(S): Carter, Malcolm Clive; Cockerill, George Stuart; Guntrip, Stephen Barry; Lackey, Karen Elizabeth; Smith, Kathryn Jane
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

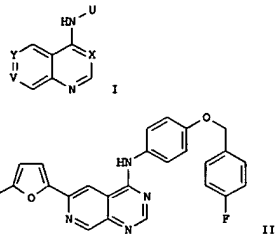
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9935146 | A1 | 19990715 | WO 1999-EP48 | 19990108 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2317589 | AA | 19990715 | CA 1999-2317589 | 19990108 |
| AU 9922783 | A1 | 19990726 | AU 1999-22783 | 19990108 |
| AU 749549 | B2 | 20020627 | | |
| BR 9906904 | A | 20001017 | BR 1999-6904 | 19990108 |
| EP 1047694 | A1 | 20001102 | EP 1999-902522 | 19990108 |
| EP 1047694 | B1 | 20040707 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| TR 200002015 | T2 | 20010122 | TR 2000-200002015 | 19990108 |
| EE 200000411 | A | 20011217 | EE 2000-411 | 19990108 |
| JP 2002500225 | T2 | 20020108 | JP 2000-527545 | 19990108 |
| JP 3390741 | B2 | 20030331 | | |
| JP 2002326990 | A2 | 20021115 | JP 2002-92102 | 19990108 |
| NZ 505456 | A | 20030630 | NZ 1999-505456 | 19990108 |
| CN 1134437 | B | 20040114 | CN 1999-803887 | 19990108 |
| AT 270670 | E | 20040715 | AT 1999-902522 | 19990108 |
| EP 1454907 | A1 | 20040908 | EP 2004-76762 | 19990108 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| EP 1460072 | A1 | 20040922 | EP 2004-76761 | 19990108 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| ES 2221354 | T3 | 20041216 | ES 1999-902522 | 19990108 |
| ZA 9900172 | A | 20000711 | ZA 1999-172 | 19990111 |
| TW 477788 | B | 20020301 | TW 1999-88100388 | 19990112 |
| US 6727256 | B1 | 20040427 | US 2000-582746 | 20000630 |
| NO 2000003561 | A | 20000911 | NO 2000-3561 | 20000711 |
| HR 2000000469 | A1 | 20010630 | HR 2000-469 | 20000712 |

L5 ANSWER 84 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

| | | | | |
|---|---|---|---|---|
| BG 104668 | A | 20010430 | BG 2000-104668 | 20000807 |
| US 2002147205 | A1 | 20021010 | US 2002-71358 | 20020208 |
| US 6713485 | B2 | 20040330 | | |
| US 2003176451 | A1 | 20030918 | US 2003-342810 | 20030115 |

PRIORITY APPLN. INFO.: GB 1998-569 A 19980112
EP 1999-902522 A3 19990108
JP 2000-527545 A3 19990108
WO 1999-EP48 W 19990108
US 2000-582746 A1 20000630

OTHER SOURCE(S): MARPAT 131:102288
GI

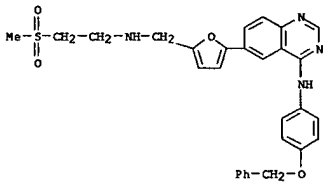


AB Title compds. I and their salts and solvates are disclosed [wherein X = N or CH; Y = CR1 and V = N; or Y = N and V = CR1; or Y = CR1 and V = CR2; or Y = CR2 and V = CR1; R1 = MeSO2CH2CH2NHCH2-Ar-, wherein Ar = (un)substituted Ph, furan, thiophene, pyrrole, or thiazole; R2 = H, halo, OH, C1-4 alkyl, C1-4 alkoxy, C1-4 alkylamino, or di[C1-4 alkyl]amino; U = Ph, pyridyl, 3H-imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, 1H-indazolyl, 2,3-dihydro-1H-indazolyl, 1H-benzimidazolyl, 2,3-dihydro-1H-benzimidazolyl or 1H-benzotriazolyl group, substituted by R3 and optionally by R4; R3 = (halo)benzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and (halo)benzyloxy, PhSO2, (trihalomethyl)benzyl, (trihalomethyl)benzyloxy, (R5)n-substituted phthalimido; R4 = OH, halo, C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl, C1-4 alkoxy, (di)(alkyl)amino, C1-4 alkylthio, etc.; R5 = halo, C1-4 alkyl, C1-4 alkoxy; n = 0-3]. Also disclosed are methods for their preparation, pharmaceutical compns. containing them, and their use in medicine. The compds. are inhibitors of protein tyrosine kinases, and as such are useful in the treatment of **cancer**, psoriasis, and rheumatoid arthritis. Over 40 title compds. and numerous intermediates were prepared For example, 4,6-dichloropyrido[3,4-d]pyrimidine was condensed with 4-[(4-fluorobenzyl)oxy]aniline at the 4-chloro position, followed by Pd-catalyzed coupling with 5-(1,3-dioxolan-2-yl)-2-(tributylstannyl)furan at the 6-chloro position, hydrolysis of the dioxolane protecting group to give an aldehyde, reductive amination of the latter with MeSCH2CH2NH2, and finally S-oxidn. with Oxone ® and acidification, to give title salt II.2HCl. In a methylene blue growth inhibition assay against 5 **tumor** cell lines, II.2HCl had an IC50 of < 5 μM against 4 of them, and an IC50 of 25-50 μM against the 5th.

IT **231277-68-2P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(target compound, metabolism; preparation of quinazolinamines and analogs as protein tyrosine kinase inhibitors)

RN 231277-68-2 CAPLUS

CN 4-Quinazolinamine, 6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-N-[4-(phenylmethoxy)phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

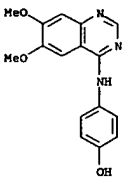
L5 ANSWER 85 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:428003 CAPLUS
DOCUMENT NUMBER: 131:295193
TITLE: Structure-based design of specific inhibitors of janus kinase 3 as apoptosis-inducing antileukemic agents
AUTHOR(S): Sudbeck, Elise A.; Liu, Xing-Ping; Narla, Rama Krishna; Mahajan, Sandeep; Ghosh, Sutapa; Mao, Chen; Uckun, Fatih M.
CORPORATE SOURCE: Parker Hughes Cancer Center, Hughes Institute, St. Paul, MN, 55113, USA
SOURCE: Clinical Cancer Research (1999), 5(6), 1569-1582
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel homol. model of the kinase domain of Janus kinase (JAK) 3 was used for the structure-based design of dimethoxyquinazoline compds. with potent and specific inhibitory activity against JAK3. The active site of JAK3 in this homol. model measures roughly 8 Å + 11 Å + 20 Å, with a volume of .apprx.530 Å3 available for inhibitor binding. Modeling studies indicated that 4-(phenylamino)-6,7-dimethoxyquinazoline (WHI-258) (I)would likely fit into the catalytic site of JAK3 and that derivs. of I that contain an OH group at the 4' position of the Ph ring would more strongly bind to JAK3 because of added interactions with Asp-967, a key residue in the catalytic site of JAK3. These predictions were consistent with docking studies indicating that compds. containing a 4-OH group, WHI-P131 [4-((4-hydroxyphenyl)amino)-6,7-dimethoxyquinazoline], WHI-P154 [4-((3-bromo-4-hydroxyphenyl)amino)-6,7-dimethoxyquinazoline], and WHI-P97 [4-((3,5-dibromo-4-hydroxyphenyl)amino)-6,7-dimethoxyquinazoline], were likely to bind favorably to JAK3, with estimated Kis ranging from 0.6 to 2.3 μM. These compds. inhibited JAK3 in immune complex kinase assays in a dose-dependent fashion. In contrast, compds. lacking the 4-OH group, WHI-P79 [4-((3-bromophenyl)amino)-6,7-dimethoxyquinazoline], WHI-P111 [4-((3-bromo-4-methylphenyl)amino)-6,7-dimethoxyquinazoline], WHI-P112 [4-((2,5-dibromophenyl)amino)-6,7-dimethoxyquinazoline], WHI-P132 [4-((2-hydroxyphenyl)amino)-6,7-dimethoxyquinazoline], and WHI-P258 [4-(phenylamino)-6,7-dimethoxyquinazoline], were predicted to bind less strongly, with estimated Kis ranging from 28 to 72 μM. These compds. did not show any significant JAK3 inhibition in kinase assays. Furthermore, the lead dimethoxyquinazoline compound, WHI-P131, which showed potent JAK3-inhibitory activity (IC50 of 78 μM), did not inhibit JAK1 and JAK2, the ZAP/SYK family tyrosine kinase SYK, the TEC family tyrosine kinase BTK, the SRC family tyrosine kinase LYN, or the receptor family tyrosine kinase insulin receptor kinase, even at concns. as high as 350 μM. WHI-P131 induced apoptosis in JAK3-expressing human leukemia cell lines NALM-6 and LC1;19 but not in melanoma (M24-MET) or squamous carcinoma (SQ20B) cells. Leukemia cells were not killed by dimethoxyquinazoline compds. that were inactive against JAK3. WHI-P131 inhibited the clonogenic growth of JAK3-pos. leukemia cell lines DAUDI, RAMOS, LC1;19, NALM-6, MOLT-3, and HL-60 (but not JAK3-neg. BT-20 breast **cancer**, M24-MET melanoma, or SQ20B squamous carcinoma cell lines) in a concentration-dependent fashion. Potent and specific inhibitors of JAK3 such as WHI-P131 may provide the basis for the design of new treatment strategies against acute lymphoblastic leukemia, the most common form of childhood **cancer**

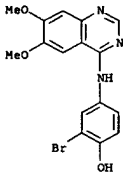
IT **202475-60-3**, WHI-P131
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(structure-based design of specific inhibitors of janus kinase 3 as

L5 ANSWER 85 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
apoptosis-inducing antileukemic agents)
RN 202475-60-3 CAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 86 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:242184 CAPLUS
DOCUMENT NUMBER: 131:72658
TITLE: Genetic and Biochemical Evidence for a Critical Role of Janus Kinase (JAK)-3 in Mast Cell-Mediated Type I Hypersensitivity Reactions
AUTHOR(S): Malaviya, Ravi; Uckun, Fatih M.
CORPORATE SOURCE: Department of Allergy, Hughes Institute, St. Paul, MN, USA
SOURCE: Biochemical and Biophysical Research Communications (1999), 257(3), 807-813
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We investigated the role of JAK3 in IgE receptor/FcεRI-mediated mast cell responses. IgE/antigen induced degranulation and mediator release were substantially reduced with Jak3-/- mast cells from JAK3-null mice that were generated by targeted disruption of Jak3 gene in embryonic stem cells. Further, treatment of mast cells with (3'bromo-4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P154), a potent inhibitor of JAK3, inhibited degranulation and proinflammatory mediator release after IgE receptor/ FcεRI crosslinking. Thus, JAK3 plays a pivotal role in IgE receptor/ FcεRI-mediated mast cell responses and targeting JAK3 may provide the basis for new and effective treatment as well as prevention programs for mast cell-mediated allergic reactions. (c) 1999 Academic Press.
IT 211555-04-3, Whi-p154
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(genetic and biochem. evidence for critical role of Janus Kinase (JAK)-3 in mast cell-mediated type I hypersensitivity reactions and inhibition by)
RN 211555-04-3 CAPLUS
CN Phenol, 2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

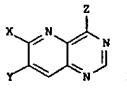


REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 87 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:113672 CAPLUS
DOCUMENT NUMBER: 130:182476
TITLE: Preparation of heterocyclic compounds as irreversible bicyclic inhibitors of tyrosine kinases
INVENTOR(S): Bridges, Alexander James
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

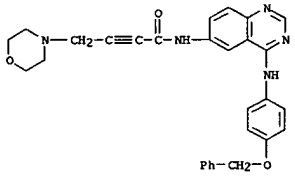
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9906396 | A1 | 19990211 | WO 1998-US15592 | 19980729 |
| W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9886659 | A1 | 19990222 | AU 1998-86659 | 19980729 |
| US 6153617 | A | 20001128 | US 1999-269647 | 19990325 |
| US 2003087881 | A1 | 20030508 | US 2002-272651 | 20021017 |
| PRIORITY APPLN. INFO.: | | | US 1997-54061P | P 19970729 |
| | | | WO 1998-US15592 | W 19980729 |
| | | | US 1999-269647 | A3 19990325 |
| | | | US 2000-656331 | B1 20000906 |

OTHER SOURCE(S): MARPAT 130:182476
GI



AB The title compds., e.g. I [X = DEF, Y = SR4, etc. ; or X = SR4, etc., and Y = DEF; D = O, etc.; E = CO, etc.; F = CR1(:C):C(R5)H, etc.; a proviso is given; R1 = H, halo, etc.; R5 = H, halo, perfluoroalkyl, etc.; Z = indoline moiety (generic structure given), etc.; R4 = H, alkyl, etc.], are prepared This invention also provides a method of treating cancer , restenosis, atherosclerosis, endometriosis, and psoriasis and a pharmaceutical composition that comprises a compound that is an irreversible inhibitor of tyrosine kinases. N-[4-(6-bromo-2,3-dihydroindol-1-yl)quinazolin-6-yl]acrylamide in vitro showed IC50 of 0.4 nM against epidermal growth factor receptor tyrosine kinase.
IT 220488-73-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. as irreversible bicyclic inhibitors of

L5 ANSWER 87 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
tyrosine kinases)
RN 220488-73-3 CAPLUS
CN 2-Butynamide, 4-(4-morpholinyl)-N-[4-[[4-(phenylmethoxy)phenyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



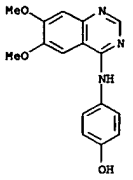
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 88 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:698779 CAPLUS
DOCUMENT NUMBER: 130:104886
TITLE: Inhibition of human glioblastoma cell adhesion and invasion by 4-(4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P131) and 4-(3'-bromo-4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P154)
AUTHOR(S): Narla, Rama Krishna; Liu, Xing-Ping; Klis, Daniel; Uckun, Fatih M.
CORPORATE SOURCE: Drug Discovery Program, Department of Experimental Oncology, Wayne Hughes Institute, St. Paul, MN, 55113, USA
SOURCE: Clinical Cancer Research (1998), 4(10), 2463-2471
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Glioblastoma multiforme is a highly invasive primary brain tumor with a disappointingly high local recurrence rate and mortality despite intensive multimodality treatment programs. Therefore, new agents that are capable of inhibiting the infiltration of normal brain parenchyma by glioblastoma cells are urgently needed. Here, we show that the novel quinazoline derivs. 4-(4'hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P131) and 4-(3'-bromo-4'hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P154) are potent inhibitors of glioblastoma cell adhesion and migration. Specifically, both compds. inhibited at micromolar concns.: (a) integrin-mediated glioblastoma cell adhesion to the extracellular matrix proteins laminin, type IV collagen, and fibronectin; (b) integrin-independent epidermal growth factor-induced adhesion of glioblastoma cells to poly-L-lysine-coated tissue culture plates; (c) fetal bovine serum-induced polymerization of actin and actin stress fiber formation as well epidermal growth factor-stimulated formation of focal adhesion plaques in serum-starved glioblastoma cells; and most importantly, (d) glioblastoma cell migration in in vitro assays of tumor cell invasiveness using tumor cell spheroids and/or Matrigel-coated Boyden chambers. Further preclin. development of WHI-P131 and WHI-P154 may provide the basis for the design of more effective adjuvant chemotherapy programs for glioblastoma multiforme.

IT **202475-60-3**, WHI-P 131
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inhibition of human glioblastoma cell adhesion and invasion by the dimethoxyquinazolines WHI-P131 and WHI-P154)
RN 202475-60-3 CAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 88 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 89 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:545399 CAPLUS
DOCUMENT NUMBER: 129:175652
TITLE: Preparation of quinazolines, quinoxalines and phenylacrylonitriles capable of modulating tyrosine kinase signal transduction and particularly KDR/FLK-1 receptor signal transduction
INVENTOR(S): App, Harald; Mcmahon, Gerald M.; Tang, Peng Cho; Gazit, Aviv; Levitzki, Alexander
PATENT ASSIGNEE(S): Sugen, Inc., USA; Yissum Research Development Co. of the Hebrew University of Jerusalem
SOURCE: U.S., 20 pp., Cont.-in-part of U. S. 5,712,395.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5792771 | A | 19980811 | US 1995-462391 | 19950605 |
| CA 2149298 | AA | 19940526 | CA 1993-2149298 | 19931115 |
| EP 1378570 | A1 | 20040107 | EP 2003-9148 | 19931115 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| US 6177401 | B1 | 20010123 | US 1994-193829 | 19940209 |
| US 5712395 | A | 19980127 | US 1995-386021 | 19950209 |
| PRIORITY APPLN. INFO.: | | | US 1992-975750 B2 | 19921113 |
| | | | US 1993-38596 B2 | 19930326 |
| | | | US 1994-193829 A2 | 19940209 |
| | | | US 1995-386021 A2 | 19950209 |
| | | | EP 1994-900810 A3 | 19931115 |

OTHER SOURCE(S): MARPAT 129:175652
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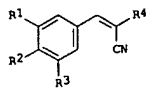

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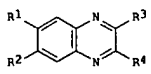
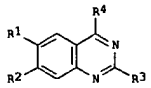


II

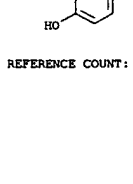


III

AB The title compds. [I, (R1 = iPr, tBu, I, etc.; R2 = OH; R3 = iPr, tBu, OH, etc.; R4 = (1-phenyl)-n-propylaminocarbonyl, cyanomethylsulfonyl, etc.), II (R1, R2 = Me, H; R1R2 = benzo; R3 = H, CHO, Cl; R4 = Ph, 3,4-(HO)2C6H4, (4-IC6H4)NH, etc.), III (R1 = MeO, Me, H; R2 = MeO; R3 = H, Cl; R4 = (3-ClC6H4)NH, (4-MeC6H4)S, (4-IC6H4)NH, etc.), etc.], capable of modulating tyrosine kinase signal transduction and particularly KDR/FLK-1 receptor signal transduction in order to regulate and/or modulate vasculogenesis and angiogenesis, were prepd. Thus, reaction of 3,5-di-tert-butyl-4-hydroxybenzaldehyde with thiocyanoacetamide and β-alanine in EtOH afforded 54% (E)-I [R1, R3 = tBu; R2 = OH; R4 = C(S)NH2] which showed IC50 of 0.8 μM against protein tyrosine kinase at the FLK-1 receptor. The invention is based, in part, on the demonstration that KDR/FLK-1 tyrosine kinase receptor expression is assocd. with endothelial cells and the identification of vascular endothelial growth factor (VEGF) as the high affinity ligand of FLK-1. These results indicate a major role for KDR/FLK-1 in the signaling system during vasculogenesis and angiogenesis. Engineering of host cells that express FLK-1 and the uses of expressed FLK-1 to evaluate and screen for drugs and analogs of VEGF involved in FLK-1 modulation by either agonist or antagonist activities is also described. The invention also relates to the use of the disclosed compds. in the treatment of disorders, including **cancer, diabetes**, diabetic retinopathy, rheumatoid arthritis, hemangioma and Kaposi's sarcoma, which are related to vasculogenesis and angiogenesis.

L5 ANSWER 89 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

IT **168835-92-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazolines, quinoxalines and phenylacrylonitriles capable of modulating tyrosine kinase signal transduction and particularly KDR/FLK-1 receptor signal transduction)
RN 168835-92-5 CAPLUS
CN Phenol, 3-[(6-methyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



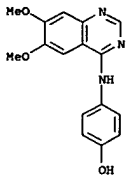
REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 90 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:401227 CAPLUS
DOCUMENT NUMBER: 129:170172
TITLE: 4-(3'-Bromo-4'hydroxylphenyl)-amino-6,7-dimethoxyquinazoline: a novel quinazoline derivative with potent cytotoxic activity against human glioblastoma cells
AUTHOR(S): Narla, Rama Krishna; Liu, Xing-Ping; Myers, Dorothea E.; Uckun, Fatih M.
CORPORATE SOURCE: Department of Experimental Oncology, Hughes Institute, St. Paul, MN, 55113, USA
SOURCE: Clinical Cancer Research (1998), 4(6), 1405-1414
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The novel quinazoline derivative 4-(3'-bromo-4'-hydroxylphenyl)-amino-6,7-dimethoxyquinazoline (WHI-P154) exhibited significant cytotoxicity against U373 and U87 human glioblastoma cell lines, causing apoptotic cell death at micromolar concns. The in vitro antiglioblastoma activity of WHI-P154 was amplified >200-fold and rendered selective by conjugation to recombinant human epidermal growth factor (EGF). The EGF-P154 conjugate was able to bind to and enter target glioblastoma cells within 10-30 min via receptor (R)-mediated endocytosis by inducing internalization of the EGF-R mols. In vitro treatment with EGF-P154 resulted in killing of glioblastoma cells at nanomolar concns. with an IC50 of 813 ± 139 nM, whereas no cytotoxicity against EGF-R-neg. leukemia cells was observed, even at concns. as high as 100 μM. The in vivo administration of EGF-P154 resulted in delayed **tumor** progression and improved **tumor**-free survival in a severe combined immunodeficient mouse glioblastoma xenograft model. Whereas none of the control mice remained alive **tumor**-free beyond 33 days (median **tumor**-free survival, 19 days) and all control mice had tumors that rapidly progressed to reach an average size of >500 mm3 by 58 days, 40% of mice treated for 10 consecutive days with 1 mg/kg/day EGF-P154 remained alive and free of detectable tumors for more than 58 days with a median **tumor**-free survival of 40 days. The tumors developing in the remaining 60% of the mice never reached a size >50 mm3. Thus, targeting WHI-P154 to the EGF-R may be useful in the treatment of glioblastoma multiforme.

IT **202475-60-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(glioblastoma inhibition by quinazoline derivative WHI-P154 targeting of EGF receptor)
RN 202475-60-3 CAPLUS
CN Phenol, 4-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 90 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

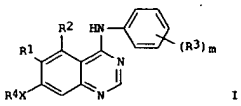


REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

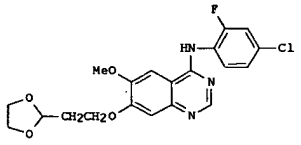
L5 ANSWER 91 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:219675 CAPLUS
DOCUMENT NUMBER: 128:257441
TITLE: Preparation of quinazoline derivatives and pharmaceutical compositions containing them
INVENTOR(S): Thomas, Andrew Peter; Hennequin, Laurent Francois Andre; Johnstone, Craig; Stokes, Elaine Sophie Elizabeth; Lohmann, Jean Jacques Marcel; Clayton, Edward
PATENT ASSIGNEE(S): Zeneca Ltd., UK; Zeneca Pharma S.A.; Thomas, Andrew Peter; Hennequin, Laurent Francois Andre; Johnstone, Craig; Stokes, Elaine Sophie Elizabeth; Lohmann, Jean Jacques Marcel; Clayton, Edward
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9813354 | A1 | 19980402 | WO 1997-GB2588 | 19970923 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| ZA 9708553 | A | 19980325 | ZA 1997-8553 | 19970923 |
| CA 2263319 | AA | 19980402 | CA 1997-2263319 | 19970923 |
| AU 9745613 | A1 | 19980417 | AU 1997-45613 | 19970923 |
| AU 729968 | B2 | 20010215 | | |
| EP 929530 | A1 | 19990721 | EP 1997-943954 | 19970923 |
| EP 929530 | B1 | 20021120 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| BR 9711302 | A | 19990817 | BR 1997-11302 | 19970923 |
| CN 1231662 | A | 19991013 | CN 1997-198133 | 19970923 |
| NZ 334014 | A | 20001027 | NZ 1997-334014 | 19970923 |
| JP 2001500891 | T2 | 20010123 | JP 1998-515387 | 19970923 |
| JP 3438818 | B2 | 20030818 | | |
| IL 129038 | A1 | 20021110 | IL 1997-129038 | 19970923 |
| AT 228114 | E | 20021215 | AT 1997-943954 | 19970923 |
| RU 2198879 | C2 | 20030220 | RU 1999-108663 | 19970923 |
| SK 283175 | B6 | 20030304 | SK 1999-389 | 19970923 |
| PT 929530 | T | 20030331 | PT 1997-943954 | 19970923 |
| ES 2185999 | T3 | 20030501 | ES 1997-943954 | 19970923 |
| JP 2003238539 | A2 | 20030827 | JP 2003-79216 | 19970923 |
| TW 520364 | B | 20030211 | TW 1997-86113896 | 19970924 |
| NO 9901422 | A | 19990324 | NO 1999-1422 | 19990324 |
| KR 2000048572 | A | 20000725 | KR 1999-702499 | 19990324 |
| US 6414148 | B1 | 20020702 | US 1999-269595 | 19990325 |
| HK 1019332 | A1 | 20030905 | HK 1999-104114 | 19990922 |
| US 2002173646 | A1 | 20021121 | US 2002-80716 | 20020225 |
| US 6673803 | B2 | 20040106 | | |
| JP 2004002406 | A2 | 20040108 | JP 2003-120734 | 20030320 |
| US 2004242574 | A1 | 20041202 | US 2003-698388 | 20031103 |
| PRIORITY APPLN. INFO.: | | | EP 1996-402033 A | 19960925 |
| | | | EP 1997-401042 A | 19970509 |
| | | | JP 1998-515387 A3 | 19970923 |
| | | | WO 1997-GB2588 W | 19970923 |
| | | | US 1999-269595 A3 | 19990325 |
| | | | US 2002-80716 A1 | 20020225 |

OTHER SOURCE(S): MARPAT 128:257441
GI



I

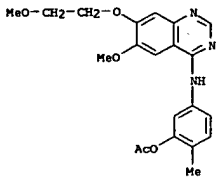


II

AB Quinazoline derivs. of formula I [R1 = H, OH, halo, NO2, alkyl, etc.; R2 = H, OH, halo, OMe, NH2, NO2; R3 = OH, halo, alkyl, alkoxy, acyloxy, CF3, CN, NH2, NO2; m = 1-2; X = O, CH2, S, SO, SO2, etc.; R4 = heterocyclo-alkyl, cycloalkyl, etc.] are prepared These compds. and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including **cancer** and rheumatoid arthritis. Thus, 2-(2-bromoethyl)-1,3-dioxolane is added to 4-(4-chloro-2-fluoroanilino)-7-hydroxy-6-methoxyquinazoline (preparation given) to give II. Pharmaceutical compns. containing I are described.

IT **196603-83-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline derivs. as antitumor, antiangiogenic and antiarthritic agents)
RN 196603-83-5 CAPLUS
CN Phenol, 5-[[6-methoxy-7-(2-methoxyethoxy)-4-quinazolinyl]amino]-2-methyl-, acetate (ester) (9CI) (CA INDEX NAME)

L5 ANSWER 91 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 92 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:146697 CAPLUS
DOCUMENT NUMBER: 128:213386
TITLE: Protein tyrosine kinase aryl and heteroaryl quinazoline compounds having selective inhibition of her-2 autophosphorylation properties
INVENTOR(S): Myers, Michael R.; Spada, Alfred P.; Maguire, Martin P.; Persons, Paul E.
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SOURCE: U.S., 11 pp., Cont.-in-part of U.S. 5,480,883. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5721237 | A | 19980224 | US 1995-469147 | 19950606 |
| US 5480883 | A | 19960102 | US 1993-166199 | 19931210 |
| US 5656643 | A | 19970812 | US 1995-385258 | 19950208 |
| CA 2223016 | AA | 19961212 | CA 1996-2223016 | 19960606 |
| CA 2223016 | C | 20030520 | | |
| WO 9639145 | A1 | 19961212 | WO 1996-US9606 | 19960606 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML | | | | |
| AU 9661044 | A1 | 19961224 | AU 1996-61044 | 19960606 |
| AU 696456 | B2 | 19980910 | | |
| EP 831831 | A1 | 19980401 | EP 1996-918362 | 19960606 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| BR 9608638 | A | 19990629 | BR 1996-8638 | 19960606 |
| JP 11507355 | T2 | 19990629 | JP 1997-501889 | 19960606 |
| CZ 289338 | B6 | 20020116 | CZ 1997-3503 | 19960606 |

PRIORITY APPLN. INFO.:

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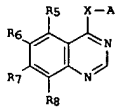
|---|---|---|
| US 1991-698420 | B2 | 19910510 |
| US 1992-988515 | B2 | 19921210 |
| US 1993-166199 | A2 | 19931210 |
| US 1993-146072 | A3 | 19931108 |
| US 1995-469147 | A | 19950606 |
| WO 1996-US9606 | W | 19960606 |

OTHER SOURCE(S): MARPAT 128:213386
GI



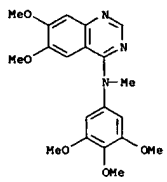
I

L5 ANSWER 92 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

AB Quinazolines I [A = (un)substituted Ph, pyrrolyl, thienyl, furyl, thiazolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, isothiazolyl, isoxazolyl, oxazolyl; X = bond, O, S, SO, SO2, OCH2, CR4:CR4, C.tplbond.C, NR4,NR4CH2; R4 = H, alkyl, aralkyl; R5-R8 = H, alkoxy, aralkoxy] are useful for the selective treatment of cell growth and differentiation characterized by activity of the epidermal growth factor receptor type 2 (her-2). Pharmaceutical compns. containing I are also described. An example is given for the preparation of 4-(3-chlorophenoxy)-6,7-dimethoxyquinazoline from 3-chlorophenol and 4-chloro-6,7-dimethoxyquinazoline.

IT **167410-48-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(epidermal growth factor receptor autophosphorylation-inhibiting quinazolines for cell **proliferation** regulation)

RN 167410-48-2 CAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-N-methyl-N-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 93 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

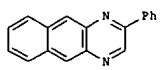
ACCESSION NUMBER: 1998:115367 CAPLUS
DOCUMENT NUMBER: 128:154102
TITLE: Quinazolines, quinoxalines, acrylonitriles, and other compounds for the treatment of disorders related to vasculogenesis and/or angiogenesis
INVENTOR(S): App, Harald; McMahon, Gerald M.; Tang, Peng Cho; Gazit, Aviv; Levitzki, Alexander
PATENT ASSIGNEE(S): Yissum Research Development Corp., Israel; Sugen
SOURCE: U.S., 16 pp., Cont.-in-part of U.S. Ser. No. 193,829, abandoned. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5712395 | A | 19980127 | US 1995-386021 | 19950209 |
| CA 2149298 | AA | 19940526 | CA 1993-2149298 | 19931115 |
| EP 1378570 | A1 | 20040107 | EP 2003-9148 | 19931115 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| US 6177401 | B1 | 20010123 | US 1994-193829 | 19940209 |
| US 5763441 | A | 19980609 | US 1995-462046 | 19950605 |
| US 5792771 | A | 19980811 | US 1995-462391 | 19950605 |
| US 5981569 | A | 19991109 | US 1995-463247 | 19950605 |
| US 5849742 | A | 19981215 | US 1997-853239 | 19970509 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1992-975750 | B2 | 19921113 |
| US 1993-38596 | B2 | 19930326 |
| US 1994-193829 | B2 | 19940209 |
| EP 1994-900810 | A3 | 19931115 |
| US 1995-386021 | A2 | 19950209 |

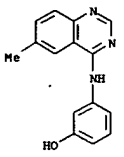
OTHER SOURCE(S): MARPAT 128:154102
GI



I

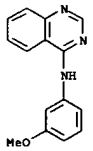
AB The invention relates to a wide variety of organic mols. capable of modulating tyrosine kinase signal transduction, and particularly KDR/FLK-1 receptor signal transduction, in order to regulate and/or modulate vasculogenesis and angiogenesis. The invention is based, in part, on the demonstration that KDR/FLK-1 tyrosine kinase receptor expression is associated with endothelial cells, and the identification of vascular endothelial growth factor (VEGF) as the high-affinity ligand of FLK-1. These results indicate a major role for KDR/FLK-1 in the signaling system during vasculogenesis and angiogenesis. Engineering of host cells that express FLK-1 and the uses of expressed FLK-1 to evaluate and screen for drugs and analogs of VEGF involved in FLK-1 modulation by either agonist or antagonist activities is also described. The invention also relates to the use of the disclosed compds. in the treatment of disorders, including **cancer, diabetes**, hemangioma and Kaposi's sarcoma, which are related to vasculogenesis and angiogenesis. Examples include prepns. of about 30 title compds., and a variety of bioassays. For instance, cyclocondensation of 2,3-diaminonaphthalene with phenylglyoxal in

L5 ANSWER 93 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
refluxing EtOH gave 65% of the claimed title compd. 2-phenyl-1,4-diazaanthracene (I). The latter compd. gave 41% inhibition of growth of Calu-6 human lung cancer xenografts in immunocompetent mice when given at a rate of 20 mg/kg/day.
IT 168835-92-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazolines, quinoxalines, acrylonitriles, and other compds. as vasculogenesis and/or angiogenesis inhibitors)
RN 168835-92-5 CAPLUS
CN Phenol, 3-[(6-methyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)




REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 94 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aryl and heteroaryl quinazoline compds. which inhibit EGF and/or PDGF receptor tyrosine kinase)
RN 146885-03-2 CAPLUS
CN 4-Quinazolinamine, N-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)




REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 94 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:105843 CAPLUS
DOCUMENT NUMBER: 128:136497
TITLE: Aryl and heteroaryl quinazoline compounds which inhibit EGF and/or PDGF receptor tyrosine kinase
INVENTOR(S): Myers, Michael R.; Spada, Alfred P.; Maguire, Martin P.; Persons, Paul E.
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SOURCE: U.S., 19 pp., Cont.-in-part of U.S. 5,480,883.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

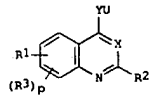
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5710158 | A | 19980120 | US 1994-229886 | 19940419 |
| US 5480883 | A | 19960102 | US 1993-166199 | 19931210 |
| WO 9515758 | A1 | 19950615 | WO 1994-US14180 | 19941208 |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN | | | | |
| RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9513050 | A1 | 19950627 | AU 1995-13050 | 19941208 |
| EP 871448 | A1 | 19981021 | EP 1995-904308 | 19941208 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE | | | | |
| EP 1488792 | A2 | 20041222 | EP 2004-19772 | 19941208 |
| EP 1488792 | A3 | 20050105 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE | | | | |
| US 5656643 | A | 19970812 | US 1995-385258 | 19950208 |
| US 6645969 | B1 | 20031111 | US 1995-521852 | 19950518 |
| US 5714493 | A | 19980203 | US 1996-652444 | 19960604 |
| US 37650 | E | 20020409 | US 2000-496399 | 20000202 |
| PRIORITY APPLN. INFO.: | | | US 1991-698420 | B2 19910510 |
| | | | US 1992-988515 | B2 19921210 |
| | | | US 1993-166199 | A2 19931210 |
| | | | WO 1992-US3736 | A2 19920506 |
| | | | US 1993-146072 | A3 19931108 |
| | | | US 1994-229886 | A 19940419 |
| | | | EP 1995-904308 | A3 19941208 |
| | | | WO 1994-US14180 | W 19941208 |
| | | | US 1996-652444 | A5 19960604 |

OTHER SOURCE(S): MARPAT 128:136497
AB This invention relates to the modulation and/or inhibition of cell signaling, cell proliferation, cell inflammatory response, the control of abnormal cell growth and cell reproduction More specifically, this invention relates to the use of mono- and/or bicyclic aryl or heteroaryl quinazoline compds. in inhibiting cell proliferation, including compds. which are useful protein tyrosine kinase (PTK) inhibitors. The method of treating cell proliferation using said quinazoline compds. and their use in pharmaceutical compns. is described. A number of compds. were tested for inhibition of PDGF receptor cell-free antophosphorylation procedure.
IT 146885-03-2

L5 ANSWER 95 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:71133 CAPLUS
DOCUMENT NUMBER: 128:140716
TITLE: Preparation of azolylquinazolines and related compounds as protein tyrosine kinase inhibitors.
INVENTOR(S): Cockerill, George Stuart; Carter, Malcolm Clive; Guntrip, Stephen Barry; Smith, Kathryn Jane
PATENT ASSIGNEE(S): Glaxo Group Limited, UK; Cockerill, George Stuart; Carter, Malcolm Clive; Guntrip, Stephen Barry; Smith, Kathryn Jane
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9802434 | A1 | 19980122 | WO 1997-EP3672 | 19970711 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| ZA 9706147 | A | 19990111 | ZA 1997-6147 | 19970710 |
| AU 9737668 | A1 | 19980209 | AU 1997-37668 | 19970711 |
| EP 912559 | A1 | 19990506 | EP 1997-934458 | 19970711 |
| EP 912559 | B1 | 20021106 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2000514806 | T2 | 20001107 | JP 1998-505596 | 19970711 |
| AT 227283 | E | 20021115 | AT 1997-934458 | 19970711 |
| PT 912559 | T | 20030331 | PT 1997-934458 | 19970711 |
| ES 2186908 | T3 | 20030516 | ES 1997-934458 | 19970711 |
| US 6391874 | B1 | 20020521 | US 1998-214267 | 19981231 |
| US 2002147214 | A1 | 20021010 | US 2002-62647 | 20020131 |
| US 6828320 | B2 | 20041207 | | |
| PRIORITY APPLN. INFO.: | | | GB 1996-14755 | A 19960713 |
| | | | GB 1996-25458 | A 19961207 |
| | | | WO 1997-EP3672 | W 19970711 |
| | | | US 1998-214267 | A1 19981231 |

OTHER SOURCE(S): MARPAT 128:140716
GI




I

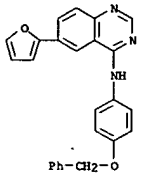
AB Title compds. [I; U = substituted Ph, mono- or bicyclic 5-10 membered (hetero)cyclyl; X = N, CH; Y = W(CH2), (CH2)W, W; W = O, S(O)m, NRa; Ra =

L5 ANSWER 95 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
H, alkyl; m = 0-2; R1 = (substituted) Ph, 5- or 6-membered heterocyclyl contg. 1-4 heteroatoms selected from N, O, S(O)n; with the provision that the ring does not contain two adjacent O or S(O)m atoms and that where the ring contains only N as heteroatom(s) the ring is C-linked to the quinazoline or quinoline ring; R3 = H, amino, halo, OH, NO2, CO2H, CHO, cyano, CF3, OCF3, carbamoyl, alkoxycarbonyl, Ph, PhO, pyridonyl, pyrrolidinyl, imidazolyl, dioxolanyl, arylsulfonyl, alkylsulfonyl, alkylcarbamoylalkyl, piperidinoalkoxy, thiomorpholino, etc.; 2 adjacent R3 = methylenedioxy, ethylenedioxy; p = 0-3], were prepd. Thus, (S)-1-{5-[4-(1-benzyl-1H-indazol-5-ylamino)quinazolin-6-yl]furan-2-ylmethyl}pyrrolidine-2-carboxylic acid amide dihydrochloride (prepn. given) inhibited BT474 human breast cancer cell proliferation with IC50 = 2 nM.

IT **202196-33-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of azolylquinazolines and related compds. as protein tyrosine kinase inhibitors)

RN 202196-33-6 CAPLUS

CN 4-Quinazolinamine, 6-(2-furanyl)-N-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 96 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

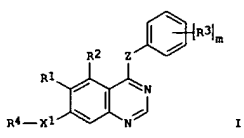
ACCESSION NUMBER: 1997:675952 CAPLUS
DOCUMENT NUMBER: 127:262698
TITLE: Preparation of quinazolines as VEGF inhibitors
INVENTOR(S): Thomas, Andrew Peter; Johnstone, Craig; Hennequin, Laurent Francois Andre
PATENT ASSIGNEE(S): Zeneca Ltd., UK; Zeneca Pharma S.A.; Thomas, Andrew Peter; Johnstone, Craig; Hennequin, Laurent Francois Andre
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9730035 | A1 | 19970821 | WO 1997-GB365 | 19970210 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2242425 | AA | 19970821 | CA 1997-2242425 | 19970210 |
| AU 9717290 | A1 | 19970902 | AU 1997-17290 | 19970210 |
| AU 719434 | B2 | 20000511 | | |
| EP 880508 | A1 | 19981202 | EP 1997-904512 | 19970210 |
| EP 880508 | B1 | 20030416 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| CN 1211239 | A | 19990317 | CN 1997-192221 | 19970210 |
| CN 1125817 | B | 20031029 | | |
| BR 9707495 | A | 19990727 | BR 1997-7495 | 19970210 |
| NZ 330868 | A | 20000128 | NZ 1997-330868 | 19970210 |
| JP 2000504714 | T2 | 20000418 | JP 1997-529078 | 19970210 |
| IL 125686 | A1 | 20021110 | IL 1997-125686 | 19970210 |
| RU 2196137 | C2 | 20030110 | RU 1998-117074 | 19970210 |
| CZ 291386 | B6 | 20030212 | CZ 1998-2535 | 19970210 |
| AT 237596 | E | 20030515 | AT 1997-904512 | 19970210 |
| PT 880508 | T | 20030731 | PT 1997-904512 | 19970210 |
| ES 2194181 | T3 | 20031116 | ES 1997-904512 | 19970210 |
| ZA 9701180 | A | 19970813 | ZA 1997-1180 | 19970212 |
| TW 581765 | B | 20040401 | TW 1997-86101670 | 19970212 |
| NO 9803687 | A | 19980813 | NO 1998-3687 | 19980812 |
| US 6184225 | B1 | 20010206 | US 1998-125271 | 19980813 |
| HK 1016607 | A1 | 20030926 | HK 1999-101774 | 19990421 |

PRIORITY APPLN. INFO.: EP 1996-400293 A 19960213
EP 1996-401756 A 19960808
EP 1996-402764 A 19961217
WO 1997-GB365 W 19970210

OTHER SOURCE(S): MARPAT 127:262698
GI

L5 ANSWER 96 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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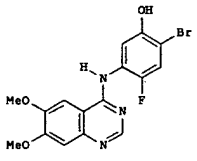


II

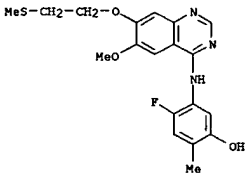
AB The title compds. [I; Z = O, NH, S; m = 1-5; R1 = H, OH, halo, etc.; R2 = H, OH, halo, etc.; R3 = OH, halo, C1-3 alkyl, etc.; X1 = O, CH2, S, etc.; R4 = H, C1-5 alkyl, C1-5 hydroxyalkyl, etc.] and their salts which inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including **cancer** and rheumatoid arthritis, were prepared and formulated. Thus, reaction of 4-chloro-6,7-dimethoxyquinazoline with 4-bromo-2-fluoro-5-hydroxyaniline in the presence of isopropanolic hydrogen chloride in 2-butanol afforded 87% quinazoline II.HCl. Compds. I are effective at 1-50 mg/kg.

IT **196194-02-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of quinazolines as VEGF inhibitors)

RN 196194-02-2 CAPLUS

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(methylthio)ethoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

L5 ANSWER 96 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L5 ANSWER 97 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:640511 CAPLUS
DOCUMENT NUMBER: 127:278209
TITLE: Preparation of 4-anilinoquinazolines for use in the treatment of disease states associated with antiangiogenesis and/or increased vascular permeability
INVENTOR(S): Thomas, Andrew Peter; Hennequin, Laurent Francois Andre; Johnstone, Craig
PATENT ASSIGNEE(S): Zeneca Ltd., UK; Zeneca Pharma S.A.; Thomas, Andrew Peter; Hennequin, Laurent Francois Andre; Johnstone, Craig
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9732856 | A1 | 19970912 | WO 1997-GB550 | 19970228 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| ZA 9701747 | A | 19980827 | ZA 1997-1747 | 19970227 |
| CA 2244897 | AA | 19970912 | CA 1997-2244897 | 19970228 |
| AU 9718664 | A1 | 19970922 | AU 1997-18664 | 19970228 |
| AU 719327 | B2 | 20000504 | | |
| EP 885198 | A1 | 19981223 | EP 1997-906814 | 19970228 |
| EP 885198 | B1 | 20011219 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| CN 1212684 | A | 19990331 | CN 1997-192807 | 19970228 |
| CN 1116286 | B | 20030730 | | |
| NZ 331191 | A | 20000327 | NZ 1997-331191 | 19970228 |
| JP 2000517291 | T2 | 20001226 | JP 1997-531552 | 19970228 |
| AT 211134 | E | 20020115 | AT 1997-906814 | 19970228 |
| PT 885198 | T | 20020628 | PT 1997-906814 | 19970228 |
| ES 2169355 | T3 | 20020701 | ES 1997-906814 | 19970228 |
| IL 125954 | A1 | 20030624 | IL 1997-125954 | 19970228 |
| TW 542826 | B | 20030721 | TW 1997-86102593 | 19970304 |
| NO 9804085 | A | 19980904 | NO 1998-4085 | 19980904 |
| US 6291455 | B1 | 20010918 | US 1998-142339 | 19980908 |

PRIORITY APPLN. INFO.:
EP 1996-400468 A 19960305
EP 1996-401499 A 19960708
WO 1997-GB550 W 19970228

OTHER SOURCE(S): MARPAT 127:278209
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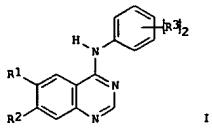
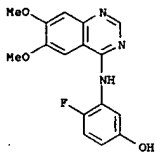
L5 ANSWER 97 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



I

AB The title compds. [I; R1 = H, MeO; R2 = MeO, EtO, 2-MeO(CH2)2O, etc.; R3 = halo, OH, CN, etc.] and their salts, inhibiting the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis, were prepared and formulated. Thus, reaction of 4-chloro-7-(2-methoxyethoxy)quinazoline.HCl with 4-chloro-2-fluoroaniline in iPrOH afforded 84% I [R1 = H; R2 = 2-MeO(CH2)2O; R3 = 4-Cl, 2-F]. Compds. I are effective at 1-50 mg/kg.
IT **196603-42-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-anilinoquinazolines for use in the treatment of disease states associated with antiangiogenesis and/or increased vascular permeability)
RN 196603-42-6 CAPLUS
CN Phenol, 3-[(6,7-dimethoxy-4-quinazolinyl)amino]-4-fluoro-, monohydrochloride (9CI) (CA INDEX NAME)



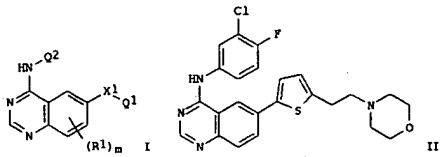
● HCl

L5 ANSWER 98 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:568090 CAPLUS
DOCUMENT NUMBER: 127:248122
TITLE: Quinazoline derivatives as antitumor agents
INVENTOR(S): Barker, Andrew John; Johnstone, Craig
PATENT ASSIGNEE(S): Zeneca Limited, UK
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9730034 | A1 | 19970821 | WO 1997-GB344 | 19970210 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2242102 | AA | 19970821 | CA 1997-2242102 | 19970210 |
| AU 9716126 | A1 | 19970902 | AU 1997-16126 | 19970210 |
| AU 707339 | B2 | 19990708 | | |
| EP 880507 | A1 | 19981202 | EP 1997-902496 | 19970210 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| CN 1211240 | A | 19990317 | CN 1997-192242 | 19970210 |
| JP 2000504713 | T2 | 20000418 | JP 1997-529073 | 19970210 |
| NZ 330816 | A | 20000526 | NZ 1997-330816 | 19970210 |
| IL 125685 | A1 | 20021110 | IL 1997-125685 | 19970210 |
| ZA 9701231 | A | 19970814 | ZA 1997-1231 | 19970213 |
| US 5866572 | A | 19990202 | US 1997-796483 | 19970213 |
| NO 9803707 | A | 19981013 | NO 1998-3707 | 19980813 |
| US 6399602 | B1 | 20020604 | US 1998-152070 | 19980911 |
| US 2003018029 | A1 | 20030123 | US 2002-136276 | 20020502 |

PRIORITY APPLN. INFO.:
GB 1996-3095 A 19960214
WO 1997-GB344 W 19970210
US 1997-796483 A3 19970213
US 1998-152070 A1 19980911

OTHER SOURCE(S): MARPAT 127:248122
GI

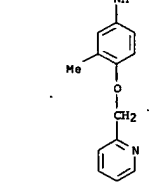


I



II

L5 ANSWER 98 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
AB The invention concerns quinazoline derivs. I [X1 = bond, CO, C(R2)2, CH(OR2), S, C.tplbond.C, O, S, etc.; Q1 = Ph, naphthyl, or 5- or 6-membered heteroaryl optionally bearing 1-3 substituents; m = 1 or 2; R1 = H, halo, CF3, OH, NH2, cyano, etc.; R2 = H, alkyl; Q2 = Ph or 9- or 10-membered bicyclic heterocycle optionally bearing 1-3 substituents] and their pharmaceutically acceptable salts. Also disclosed are processes for preparation of I and salts, pharmaceutical compns. containing them, and the use of their receptor tyrosine kinase inhibitory properties in the treatment of proliferative diseases such as cancer. Examples include syntheses of 40 compds. and various intermediates. For instance, Pd(PPh3)4-catalyzed coupling of 6-bromo-4-(3-chloro-4-fluoroanilino)quinazoline-HCl with di-iso-Pr [5-(2-morpholinoethyl)thien-2-yl]boronate (prepns. given) gave 27% title compound II. At 50 mg/kg/day in athymic nude mice with human vulval epidermoid carcinoma xenografts (cell line A-431), II gave 64% inhibition of tumor volume (vs. control) after 13 days.
IT **195457-50-2P**, 4-[3-Methyl-4-(2-pyridylmethoxy)anilino]-6-(2-thienyl)quinazoline
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline derivs. as antitumor agents and antiproliferatives)
RN 195457-50-2 CAPLUS
CN 4-Quinazolinamine, N-[3-methyl-4-(2-pyridinylmethoxy)phenyl]-6-(2-thienyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 99 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

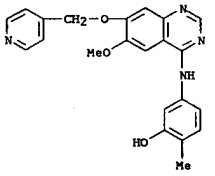
ACCESSION NUMBER: 1997:502972 CAPLUS
DOCUMENT NUMBER: 127:135808
TITLE: Preparation and antiangiogenic and/or vascular permeability reducing effect of quinazoline derivatives
INVENTOR(S): Lohmann, Jean-Jacques Marcel; Hennequin, Laurent Francois Andre; Thomas, Andrew Peter
PATENT ASSIGNEE(S): Zeneca Limited, UK; Zeneca-Pharma S.A.; Lohmann, Jean-Jacques Marcel; Hennequin, Laurent Francois Andre; Thomas, Andrew Peter
SOURCE: PCT Int. Appl., 162 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9722596 | A1 | 19970626 | WO 1996-GB3075 | 19961213 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2237005 | AA | 19970626 | CA 1996-2237005 | 19961213 |
| AU 9711061 | A1 | 19970714 | AU 1997-11061 | 19961213 |
| AU 712370 | B2 | 19991104 | | |
| EP 873319 | A1 | 19981028 | EP 1996-941787 | 19961213 |
| EP 873319 | B1 | 20010725 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| CN 1205694 | A | 19990120 | CN 1996-199110 | 19961213 |
| CN 1133625 | B | 20040107 | | |
| BR 9612043 | A | 19991228 | BR 1996-12043 | 19961213 |
| JP 2000515114 | T2 | 20001114 | JP 1997-522568 | 19961213 |
| AT 203524 | E | 20010815 | AT 1996-941787 | 19961213 |
| ES 2162656 | T3 | 20020101 | ES 1996-941787 | 19961213 |
| PT 873319 | T | 20020130 | PT 1996-941787 | 19961213 |
| SK 282443 | B6 | 20020205 | SK 1998-828 | 19961213 |
| CZ 291100 | B6 | 20021211 | CZ 1998-1882 | 19961213 |
| RU 2194701 | C2 | 20021220 | RU 1998-113300 | 19961213 |
| ZA 9610597 | A | 19970618 | ZA 1996-10597 | 19961217 |
| US 5962458 | A | 19991005 | US 1996-768887 | 19961217 |
| TW 411274 | B | 20001111 | TW 1996-85115569 | 19961217 |
| NO 9802784 | A | 19980817 | NO 1998-2784 | 19980617 |
| US 6071921 | A | 20000606 | US 1998-203764 | 19981202 |
| US 6258951 | B1 | 20010710 | US 2000-500470 | 20000209 |
| US 2002032208 | A1 | 20020314 | US 2001-877005 | 20010611 |
| US 6362336 | B2 | 20020326 | | |
| GR 3036954 | T3 | 20020131 | GR 2001-401823 | 20011019 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| EP 1995-402846 | A | 19951218 |
| EP 1996-402190 | A | 19961015 |

L5 ANSWER 99 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

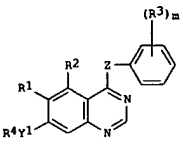


●1/5 HCl

L5 ANSWER 99 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

| | | |
|---|---|---|
| EP 1996-941787 | A | 19961213 |
| WO 1996-GB3075 | W | 19961213 |
| US 1996-768887 | A1 | 19961217 |
| US 1998-203764 | A1 | 19981202 |
| US 2000-500470 | A3 | 20000209 |

OTHER SOURCE(S): MARPAT 127:135808
GI



I

AB Quinazoline derivs. I [Y1 represents -O-, -S-, -CH2-, -SO-, -SO2-, NR5CO-, -CONR6-, -SO2NR7-, -NR8SO2- or -NR9- (wherein R5, R6, R7, R8 and R9 each independently represents hydrogen, alkyl or alkoxyalkyl); R1 represents hydrogen, hydroxy, halo, nitro, trifluoromethyl, cyano, alkyl, alkoxy, alkylthio, amino, alkylamino; R2 represents hydrogen, hydroxy, halo, alkyl, alkoxy, trifluoromethyl, cyano, amino, nitro; m is an integer from 1 to 5; R3 represents hydroxy, halo, alkyl, alkoxy, alkanoyloxy, trifluoromethyl, cyano, amino, nitro; R4 represents a group which is or which contains an optionally substituted pyridone, Ph or aromatic heterocyclic group] were prepared I inhibit the effects of VEGF (no data), a property of value in the treatment of a number of disease states including **cancer** and rheumatoid arthritis. E.g., heating a mixture of 2-amino-4-benzyloxy-5-methoxybenzamide and Gold's reagent, followed by NaOAc and HOAc, gave 7-benzyloxy-6-methoxy-3,4-dihydroquinazolin-4-one. The product was treated with thionyl chloride, then 3-acetoxy-4-methylaniline, and next hydrogenolyzed to give 4-(3-acetoxy-4-methylanilino)-7-hydroxy-6-methoxyquinazoline hydrochloride. The last was reacted with 4-(bromomethyl)pyridine hydrobromide and treated with aqueous NaOH to give 4-(3-hydroxy-4-methylanilino)-6-methoxy-7-(4-pyridylmethoxy)quinazoline hydrochloride.

IT **192999-68-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antiangiogenic and/or vascular permeability reducing effect of quinazoline derivs.)

RN 192999-68-1 CAPLUS
CN Phenol, 5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl-, hydrochloride (5:1) (9CI) (CA INDEX NAME)

L5 ANSWER 100 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:107384 CAPLUS
DOCUMENT NUMBER: 126:113167
TITLE: Protein tyrosine kinase aryl and heteroaryl quinazoline compounds having selective inhibition of HER-2 autophosphorylation properties
INVENTOR(S): Myers, Michael R.; Spada, Alfred P.; Maguire, Martin P.; Persons, Paul E.
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA; Myers, Michael R.; Spada, Alfred P.; Maguire, Martin P.; Persons, Paul, E.
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9639145 | A1 | 19961212 | WO 1996-US9606 | 19960606 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML | | | | |
| US 5656643 | A | 19970812 | US 1995-385258 | 19950208 |
| US 5721237 | A | 19980224 | US 1995-469147 | 19950606 |
| AU 9661044 | A1 | 19961224 | AU 1996-61044 | 19960606 |
| AU 696456 | B2 | 19980910 | | |
| EP 831831 | A1 | 19980401 | EP 1996-918362 | 19960606 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| BR 9608638 | A | 19990629 | BR 1996-8638 | 19960606 |
| JP 11507355 | T2 | 19990629 | JP 1997-501889 | 19960606 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1995-469147 | A | 19950606 |
| US 1991-698420 | B2 | 19910510 |
| US 1992-988515 | B2 | 19921210 |
| US 1993-146072 | A3 | 19931108 |
| US 1993-166199 | A2 | 19931210 |
| WO 1996-US9606 | W | 19960606 |

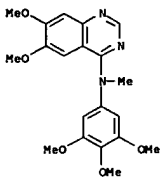
OTHER SOURCE(S): MARPAT 126:113167

AB A method is disclosed for the selective treatment of cell growth and differentiation characterized by activity of the human epidermal growth factor receptor type 2 (HER2). More specifically, this invention relates to the use of substituted or unsubstituted mono- or bi-cyclic aryl, heteroaryl, cycloalkyl or heterocycloalkyl compds. in selectively regulating cell growth. Pharmaceutical compns. useful for the selective treatment of cell growth and differentiation are also described.

IT **167410-48-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein tyrosine kinase aryl and heteroaryl quinazoline compds. with selective inhibition of HER-2 autophosphorylation properties, and compound preparation)

RN 167410-48-2 CAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-N-methyl-N-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)

L5 ANSWER 100 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L5 ANSWER 101 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

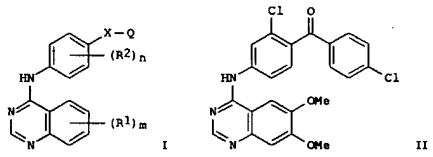
ACCESSION NUMBER: 1996:483485 CAPLUS
DOCUMENT NUMBER: 125:142741
TITLE: Preparation of N-phenyl-4-quinazolinamines for the treatment of proliferative diseases
INVENTOR(S): Brown, Dearg Sutherland; Morris, Jeffrey James; Thomas, Andrew Peter
PATENT ASSIGNEE(S): Zeneca Limited, UK
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9615118 | A1 | 19960523 | WO 1995-GB2606 | 19951108 |
| W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2200871 | AA | 19960523 | CA 1995-2200871 | 19951108 |
| AU 9538130 | A1 | 19960606 | AU 1995-38130 | 19951108 |
| AU 703328 | B2 | 19990325 | | |
| EP 790986 | A1 | 19970827 | EP 1995-936044 | 19951108 |
| EP 790986 | B1 | 19990120 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 10508616 | T2 | 19980825 | JP 1995-515816 | 19951108 |
| AT 175962 | E | 19990215 | AT 1995-936044 | 19951108 |
| ES 2128092 | T3 | 19990501 | ES 1995-936044 | 19951108 |
| ZA 9509572 | A | 19960513 | ZA 1995-9572 | 19951110 |
| IL 115959 | A1 | 20040620 | IL 1995-115959 | 19951112 |
| FI 9701970 | A | 19970507 | FI 1997-1970 | 19970507 |
| NO 9702152 | A | 19970512 | NO 1997-2152 | 19970509 |
| US 5821246 | A | 19981013 | US 1997-836362 | 19970521 |

PRIORITY APPLN. INFO.: GB 1994-22866 A 19941112
GB 1995-7308 A 19950407
WO 1995-GB2606 W 19951108

OTHER SOURCE(S): MARPAT 125:142741
GI

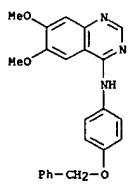
L5 ANSWER 101 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



AB The title compds. I (m = 1-3; R1 = halo, hydroxy, amino, ureido, etc.; n = 0-3; R2 = halo, trifluoromethyl, hydroxy, amino, nitri, cyano, alkyl; X = carbonyl, methine, O,S, etc.) were disclosed. I were claimed for the use as receptor tyrosine kinase inhibitors and for treatment of **proliferative** disease such as **cancer**. An example compound is the chlorophenyl [(quinazolinyl)amino]phenyl methanone II.

IT **179246-75-4P**
RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-phenylquinazolinamines as tyrosine kinase inhibitors)

RN 179246-75-4 CAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-N-[4-(phenylmethoxy)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L5 ANSWER 102 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:462220 CAPLUS
DOCUMENT NUMBER: 125:114665
TITLE: Preparation of quinoline and quinazoline protein tyrosine kinase inhibitors
INVENTOR(S): Hudson, Alan Thomas; Vile, Sadie; Barraclough, Paul; Franzmann, Karl Witold; McKeown, Stephen Carl; Page, Martin John
PATENT ASSIGNEE(S): Wellcome Foundation Limited, UK
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9609294 | A1 | 19960328 | WO 1995-GB2202 | 19950918 |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM | | | | |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9534824 | A1 | 19960409 | AU 1995-34824 | 19950918 |
| ZA 9507853 | A | 19970318 | ZA 1995-7853 | 19950918 |
| EP 782570 | A1 | 19970709 | EP 1995-931351 | 19950918 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 10505600 | T2 | 19980602 | JP 1995-509740 | 19950918 |

PRIORITY APPLN. INFO.: GB 1994-18852 A 19940919
GB 1995-7788 A 19950413
GB 1995-10757 A 19950526
WO 1995-GB2202 W 19950918

OTHER SOURCE(S): MARPAT 125:114665
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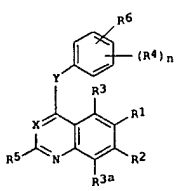


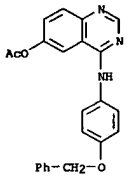
AB The title compds. [I; X = N, CH; Y = W(CH2), (CH2)W, W; W = O, S(O)m, (un)substituted NH; R1 = NH2, H, halogen, OH, NO2, CO2H, CF3, CF3O, ureido, etc.; R4 = H, OH, halogen, alkyl, alkoxy, alkylthio, CN, NO2, CF3, etc.; n = 1-3; R5 = H, halogen, CF3, alkyl, alkoxy; R6 = substituted

L5 ANSWER 102 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
hydrocarbyl, etc.], which are protein tyrosine kinase inhibitors, are prepd. Thus, 4-chloroquinoline was reacted with 4-methoxyaniline in the presence of HCl, producing 4-(4-phenoxyanilino)quinoline hydrochloride, m.p. 216-218°, which demonstrated a IC50 against p561ck protein tyrosine kinase of 5 μM.

IT **179246-80-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of quinoline and quinazoline protein tyrosine kinase inhibitors)

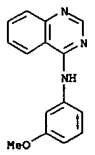
RN 179246-80-1 CAPLUS

CN 6-Quinazolinol, 4-[[4-(phenylmethoxy)phenyl]amino]-, acetate (ester), monohydrochloride (9CI) (CA INDEX NAME)




● HCl

L5 ANSWER 103 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)




L5 ANSWER 103 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:160721 CAPLUS

DOCUMENT NUMBER: 124:249673

TITLE: Specific inhibition of epidermal growth factor receptor tyrosine kinase by 4-anilinoquinazolines

AUTHOR(S): Wakeling, A. E.; Barker, A. J.; Davies, D. H.; Brown, D. S.; Green, L. R.; Cartlidge, S. A.; Woodburn, J. R.

CORPORATE SOURCE: Cancer Research Department, Zeneca Pharmaceuticals, Macclesfield/Cheshire, SK10 4TG, UK

SOURCE: Breast Cancer Research and Treatment (1996), 38(1), 67-73
CODEN: BCTRD6; ISSN: 0167-6806

PUBLISHER: Kluwer

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Since the mitogenic action of EGF is mediated by ligand-induced autophosphorylation of the EGF receptor (EGFR), and EGFR is commonly overexpressed in solid human tumors, inhibitors of receptor tyrosine kinase activity (RTK) could prove to be effective antitumor agents. Screening of a compound library using an EGF-RTK enzyme prepared from human tumor derived A431 cells identified a series of potent (IC50 <1μM) enzyme inhibitors. These inhibitors are quinazolines bearing a variety of substituted anilines at the 4-position. The most potent 4-anilinoquinazolines (IC50 = 20nM) have small non-polar meta substituents on the aniline ring, and are competitive with ATP and non-competitive with substrate. The growth inhibitory activity of these agents was assessed in vitro using KB cells (human oral squamous tumor) grown in the absence or presence of EGF. A selected compound, 4-(3-chloroanilino)quinazoline (CAQ), inhibited EGF-stimulated growth in a concentration dependent manner and complete blockade was observed at concns. (1-10 μM) which had no effect on basal growth. Selectivity of growth inhibition by CAQ was further exemplified in IGF-1-stimulated KB cells where no effect was detected at concns. which completely blocked EGF-stimulated growth. Similarly, CAQ blocked TGFα-stimulated growth in MCF-7 human breast cancer cells without affecting insulin-stimulated growth. These studies define a novel class of EGF-RTK inhibitors which are also potent and selective inhibitors of EGF-stimulated human tumor cell growth in vitro.

IT **146885-03-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anilinoquinazolines as specific inhibitors of EGF receptor tyrosine kinase and antineoplastic agents)

RN 146885-03-2 CAPLUS

CN 4-Quinazolinamine, N-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)

L5 ANSWER 104 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:71553 CAPLUS

DOCUMENT NUMBER: 124:261073

TITLE: Bis mono- and bicyclic aryl and heteroaryl compounds which inhibit EGF and/or PDGF receptor tyrosine kinase

INVENTOR(S): Spada, Alfred P.; Myers, Michael R.; Maguire, Martin P.; Persons, Paul E.

PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA

SOURCE: U.S., 33 pp. Cont.-in-part of U.S. Ser. No. 988,515, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5480883 | A | 19960102 | US 1993-166199 | 19931210 |
| US 5710158 | A | 19980120 | US 1994-229886 | 19940419 |
| WO 9515758 | A1 | 19950615 | WO 1994-US14180 | 19941208 |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN | | | | |
| RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9513050 | A1 | 19950627 | AU 1995-13050 | 19941208 |
| EP 871448 | A1 | 19981021 | EP 1995-904308 | 19941208 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE | | | | |
| EP 1488792 | A2 | 20041222 | EP 2004-19772 | 19941208 |
| EP 1488792 | A3 | 20050105 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE | | | | |
| US 5656643 | A | 19970812 | US 1995-385258 | 19950208 |
| US 5795889 | A | 19980818 | US 1995-386271 | 19950209 |
| US 5646153 | A | 19970708 | US 1995-439027 | 19950511 |
| US 6645969 | B1 | 20031111 | US 1995-521852 | 19950518 |
| US 5721237 | A | 19980224 | US 1995-469147 | 19950606 |
| US 5714493 | A | 19980203 | US 1996-652444 | 19960604 |
| US 6057320 | A | 20000502 | US 1997-881991 | 19970625 |
| US 36256 | E | 19990720 | US 1997-988005 | 19971210 |
| AU 739382 | B2 | 20011011 | AU 1999-65543 | 19991230 |
| AU 9965543 | A1 | 20000323 | | |
| US 37650 | E | 20020409 | US 2000-496399 | 20000202 |
| US 2004014774 | A1 | 20040122 | US 2003-617342 | 20030710 |

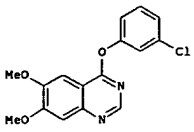
PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1991-698420 | B2 | 19910510 |
| US 1992-988515 | B2 | 19921210 |
| WO 1992-US3736 | A2 | 19920506 |
| US 1993-146072 | A3 | 19931108 |
| US 1993-166199 | A2 | 19931210 |
| US 1994-229886 | A | 19940419 |
| US 1994-299886 | B2 | 19940901 |
| EP 1995-904308 | A3 | 19941208 |
| WO 1994-US14180 | W | 19941208 |
| US 1995-439027 | A3 | 19950511 |
| US 1995-521852 | A3 | 19950518 |
| US 1996-652444 | A5 | 19960604 |

OTHER SOURCE(S): MARPAT 124:261073

GI

L5 ANSWER 104 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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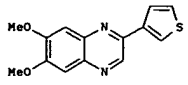


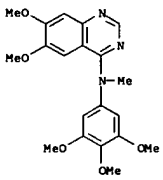
III

AB The invention relates to bis mono- and/or bicyclic aryl and/or heteroaryl compds. ArlXAr2 [I; Ar1, Ar2 = (un)substituted mono- or bicyclic rings with 0-3 substituents; X = (CHR1)0-4 or (CHR1)mZ(CHR1)n; Z = O, NR2, S, SO, SO2; m, n = 0-3; R1, R2 = H, alkyl] exhibiting protein tyrosine kinase inhibition activity. I inhibit abnormal cell **proliferation** in **proliferative** disorders by selectively inhibiting EGF and/or PDGF receptor. Approx. 300 compds. I are listed with characterizing data, and biol. data for selected compds. are given. For example, m-ClC6H4OH was treated with NaH in THF, followed by 4-chloro-6,7-dimethoxyquinazoline, to give title compound II. The claimed quinoxaline derivative III inhibited PDGF-R cell-free autophosphorylation with an IC50 of 0.02-0.05 μM.

IT **167410-48-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bis mono- and bicyclic aryl and heteroaryl compds. as protein tyrosine kinase inhibitors)

RN 167410-48-2 CAPLUS

CN 4-Quinazolinamine, 6,7-dimethoxy-N-methyl-N-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 105 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:849326 CAPLUS
DOCUMENT NUMBER: 123:246818
TITLE: Compounds for the treatment of disorders related to vasculogenesis and/or angiogenesis
INVENTOR(S): Gazit, Aviv; Levitzki, Alexander; App, Harald; Tang, Cho Peng; Mcmahon, Gerald M.
PATENT ASSIGNEE(S): Sugen, Inc., USA; Yissum Research Development Company of the Hebrew University
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9521613 | A1 | 19950817 | WO 1995-US1751 | 19950209 |
| W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN | | | | |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 6177401 | B1 | 20010123 | US 1994-193829 | 19940209 |
| AU 9518423 | A1 | 19950829 | AU 1995-18423 | 19950209 |
| EP 748219 | A1 | 19961218 | EP 1995-910239 | 19950209 |
| R: DE, FR, GB | | | | |
| JP 09508642 | T2 | 19970902 | JP 1995-521376 | 19950209 |
| JP 3202238 | B2 | 20010827 | | |

PRIORITY APPLN. INFO.:
US 1994-193829 A 19940209
US 1992-975750 B2 19921113
US 1993-38596 B2 19930326
WO 1995-US1751 W 19950209

OTHER SOURCE(S): MARPAT 123:246818

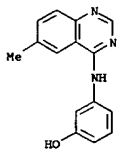
AB The present invention relates to organic mols. capable of modulating tyrosine kinase signal transduction and particularly KDR/FLK-1 receptor signal transduction in order to regulate and/or modulate vasculogenesis and angiogenesis. The invention is based, in part, on the demonstration that KDR/FLK-1 tyrosine kinase receptor expression is associated with endothelial cells and the identification of vascular endothelial growth factor (VEGF) as the high affinity ligand of FLK-1. These results indicate a major role for KDR/FLK-1 in the signaling system during vasculogenesis and angiogenesis. Engineering of host cells that express FLK-1 and the use of expressed FLK-1 to evaluate and screen for drugs and analogs of VEGF involved in FLK-1 modulation by either agonist or antagonist activities is also described. The invention also relates to the use of the disclosed compds. in the treatment of disorders, including **cancer**, **diabetes**, hemangioma and Kaposi's sarcoma, which are related to vasculogenesis and angiogenesis.

IT **168835-92-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(compds. for the treatment of disorders related to vasculogenesis and/or angiogenesis)

L5 ANSWER 105 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 168835-92-5 CAPLUS

CN Phenol, 3-[(6-methyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



L5 ANSWER 106 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

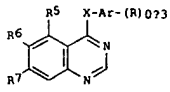
ACCESSION NUMBER: 1995:780431 CAPLUS
DOCUMENT NUMBER: 123:160872
TITLE: Aryl and heteroaryl quinazoline compounds which inhibit CSF-1R receptor tyrosine kinase
INVENTOR(S): Myers, Michael R.; Spada, Alfred P.; Maguire, Martin P.; Persons, Paul E.; Zilberstein, Asher; Hsu, Chin-Yi Jenny; Johnson, Susan E.
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9515758 | A1 | 19950615 | WO 1994-US14180 | 19941208 |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN | | | | |
| RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5480883 | A | 19960102 | US 1993-166199 | 19931210 |
| US 5710158 | A | 19980120 | US 1994-229886 | 19940419 |
| AU 9513050 | A1 | 19950627 | AU 1995-13050 | 19941208 |
| EP 871448 | A1 | 19981021 | EP 1995-904308 | 19941208 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE | | | | |
| US 5656643 | A | 19970812 | US 1995-385258 | 19950208 |
| US 6645969 | B1 | 20031111 | US 1995-521852 | 19950518 |
| US 5714493 | A | 19980203 | US 1996-652444 | 19960604 |
| US 37650 | E | 20020409 | US 2000-496399 | 20000202 |

PRIORITY APPLN. INFO.:
US 1993-166199 A 19931210
US 1994-229886 A 19940419
US 1991-698420 B2 19910510
WO 1992-US3736 A2 19920506
US 1992-988515 B2 19921210
US 1993-146072 A3 19931108
WO 1994-US14180 W 19941208
US 1996-652444 A5 19960604

OTHER SOURCE(S): MARPAT 123:160872

GI



I

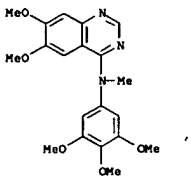
AB This invention relates to the modulation and/or inhibition of cell signaling, cell **proliferation**, cell inflammatory response, the control of abnormal cell growth and cell reproduction More specifically, this invention relates to the use of mono- and/or bicyclic aryl or heteroaryl quinazoline compds. (I; Ar = aryl or heteroaryl; X = O, S, SO, SO2, OCH2, NH, NR4, etc.; R = H, alkyl, aryl, alkenyl, OH, alkoxy, aralkoxy, aryloxy,

L5 ANSWER 106 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
halo, nitro, cyano, amino, amido, sulfonyl, halophenyl, benzoyl, etc.) in inhibiting cell **proliferation**, including compds. which are useful protein tyrosine kinase (PTK) inhibitors. The method of treating cell **proliferation** and/or differentiation or mediator release using said quinazoline compds. and their use in pharmaceutical compns. is described.

IT **167410-48-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(quinazoline compds. as inhibitors of CSF-1 receptors)

RN 167410-48-2 CAPLUS

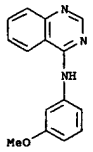
CN 4-Quinazolinamine, 6,7-dimethoxy-N-methyl-N-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)




L5 ANSWER 107 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
**use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as **neoplasm** inhibitor)

RN 146885-03-2 CAPLUS

CN 4-Quinazolinamine, N-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)

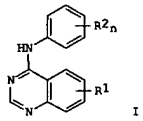



L5 ANSWER 107 OF 107 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1993:191758 CAPLUS
DOCUMENT NUMBER: 118:191758
TITLE: Preparation of 4-anilinoquinazolines as **neoplasm** inhibitors
INVENTOR(S): Barker, Andrew John; Davies, David Huw
PATENT ASSIGNEE(S): Imperial Chemical Industries PLC, UK
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 520722 | A1 | 19921230 | EP 1992-305703 | 19920622 |
| EP 520722 | B1 | 19961227 | | |
| R: AT, BE, CH, DE, DK, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE | | | | |
| ZA 9204083 | A | 19930224 | ZA 1992-4083 | 19920604 |
| CA 2071087 | AA | 19921229 | CA 1992-2071087 | 19920611 |
| HU 61290 | A2 | 19921228 | HU 1992-1964 | 19920612 |
| IL 102204 | A1 | 19970318 | IL 1992-102204 | 19920615 |
| AU 9218422 | A1 | 19930107 | AU 1992-18422 | 19920622 |
| AU 651215 | B2 | 19940714 | | |
| AT 146781 | E | 19970115 | AT 1992-305703 | 19920622 |
| NO 9202517 | A | 19921229 | NO 1992-2517 | 19920625 |
| NO 180105 | B | 19961111 | | |
| NO 180105 | C | 19970219 | | |
| JP 05208911 | A2 | 19930820 | JP 1992-167416 | 19920625 |
| PRIORITY APPLN. INFO.: | | | GB 1991-13970 A | 19910628 |
| | | | GB 1992-1133 A | 19920120 |

OTHER SOURCE(S): MARPAT 118:191758
GI




I

AB Title compds. (I; R1 = H, CF3, NO2, halo; R2 = halo, CF3, NO2, alkyl, alkoxy, etc.; n = 1 or 2) were prepared Thus, 3-BrC6H4NH2 was condensed with 4-chloroquinazoline to give I (R1 = H, R2 = 3-Br, n = 1) which had IC50 of 0.02 and 0.78 μM against receptor tyrosine kinase and growth of human nasopharyngeal cell line KB in nitro, resp.

IT **146885-03-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic**

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L3            3137 S L1 FUL

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